EXHIBIT B

Expert Overview of TVT

The following is my expert report for the Ethicon TVT Retropubic (TVT) product. The report is based on my education, training, and experience, literature reviews, journal articles, textbooks, and materials provided to me by counsel for Ethicon and Johnson & Johnson, including: company documents, reports of plaintiffs' experts and other company witness depositions. All of my opinions in this report are expressed to a reasonable degree of medical probability or certainty.

My C.V. includes a list of publications that I have authored over the past 15 years. A list of materials that I reviewed in forming my opinions is attached. I am currently being paid $500/hour to prepare a written report, $600/hour for depositions, and $725/hour for trial testimony.

I. BACKGROUND AND QUALIFICATIONS

A. Education, Scholarly Activity, and Teaching

I, Dr. Brian J. Flynn, attended the University of Rochester in Rochester, New York from 1987-1991. I graduated with a Bachelor of Science degree in Electrical Engineering with a concentration in Biomedical Engineering. I attended medical school from 1991-1995 at Temple University School of Medicine, Philadelphia, Pennsylvania and graduated with a Doctor of Medicine degree in May of 1995. I next attended Geisinger Health System, Danville, Pennsylvania for my internship and residency from 1995-2001. I completed a six-year residency in Urology. I then performed a fellowship in Reconstructive Urology, Urogynecology, and Urodynamics from July 2001-June 2002 at Duke University Medical Center under the directorship of Dr. George D. Webster. I then became a staff member at the University of Colorado School of Medicine in June 2002, where I have been on the faculty since that time.

I became a diplomate of the American Board of Urology in March 2004 and became subspecialty certified in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) in August 2014. I have had a Colorado Medical License continuously for the past 13 years. My hospital affiliations include University of Colorado Hospital, Denver Health Medical Center, Children's Hospital of Colorado, and Veteran's Administration Medical Center in Denver. My administrative activities include being the former Colorado State Representative to the South Central Section of the American Urological Association. I am the president-elect of the Rocky Mountain Urological Society. I have been the Director of a Fellowship in Reconstructive Urology at the University of Colorado School of Medicine since 2008. I am the Co-Practice Director of Women's Pelvic Health and Surgery at the University of Colorado Hospital since June 2013. I was the Assistant Residency Director of Urology at University of Colorado School of Medicine from July 2006-June 2010. I am an active member of the American Urological Association, South Central Section of the American Urological Association, Rocky

Mountain Urological Society, Society of Genitourinary Reconstructive Surgeons, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction, and International Urogynecological Association. This includes attendance at annual meetings and subscription to the associations' journals.

I review articles for the *Journal of Urology*, *International Urogynecology*, *Urology and Neurourology*, and *Urodynamics*. I have published scientific articles in peer review journals on male and female Reconstructive Urologic Surgery. I have authored instructional videos on the TVT Secur™, TVT Abbrevo™, as well as the Gynecare Prolift™ System. I have been invited to speak at a number of scientific meetings throughout the world on urogynecologic issues including incontinence, prolapse, neuromodulation, transvaginal mesh, and other female urology and urogynecology topics.

As a core faculty member of the University of Colorado School of Medicine Urology Division since 2002, I have instructed twenty-six residents on urinary incontinence and pelvic organ prolapse. Additionally, as the first and current fellowship director at the University of Colorado in pelvic medicine and reconstructive surgery, I have trained seven fellows in this specialty.

I spend 85% of my time in a clinical practice and 15% of my time in clinical research, teaching, administrative activities, medicolegal consultation, and quality improvement projects (e.g., improving bladder control and continence in multiple sclerosis patients).

I have extensive experience with transvaginal mesh and have published and presented numerous times on that topic. I am very familiar with the 2008 FDA Public Health Notification regarding transvaginal placement of surgical mesh and the FDA's 2011 update. In fact, the AUA (American Urological Association) asked me to write an update for practicing urologists on the implications of the FDA notification, as well as technical considerations of transvaginal pelvic reconstruction with polypropylene mesh. I have offered insight into prevention and management of mesh-related complications. I have proposed indications for mesh in stress urinary incontinence (SUI) and pelvic organ prolapse (POP) surgery. As a result of my education in engineering, I am certainly familiar with the biomechanical properties of polypropylene mesh. I have been invited to speak by many professional societies including the AUA, SUFU, and IUGA on the technical considerations and clinical considerations associated with transvaginal mesh.

B. Relevant Surgical Experience

I perform approximately 400 surgical cases per year, primarily at the University of Colorado Hospital. More than 50% of my practice involves Female Pelvic Medicine (FPM). In the past 13 years, I have performed more than 1,100 procedures for SUI. I have used a polypropylene mesh kit in more than 800 of these cases, including more than 500 cases using the TVT family of products.

I began assisting in incontinence procedures in 1997 when I was a urology resident. I performed a wide variety of SUI procedures, including transurethral bulking agents, Burch colposuspension, and pubovaginal sling with autografts and allografts. During my fellowship in 2001, I began performing mid-urethral slings (MUS) with polypropylene mesh under the direction of George Webster, M.D. I began my practice at the University of Colorado in 2002 and used primary American Medical Systems Sling products. In 2004, I started using primarily Ethicon's TVT product line including TVT, TVT Obturator, TVT Secur, TVT Abbrevo, and the TVT Exact.

II. URINARY INCONTINENCE (UI)

For patients to remain continent, there must be a balance between detrusor muscle activity and urethral closure. The urethral pressure will exceed bladder pressure resulting in a continent patient, and when abdominal pressures are transmitted to the urethra and bladder, the pressure differential remains favorable, leaving patients continent. Loss of support of the urethra or the disruption between the normal relationship between the lower urinary tract components leads to incontinence. SUI may be caused by pregnancy and childbirth, general loss of pelvic muscle tone (often with aging), hysterectomy, nerve and muscle damage as result of (birth) injury or surgical trauma, obesity, menopause, chronic coughing due to smoking and lung disease, anatomical predisposition, and repeated heavy lifting or activities causing impacts.

There are different forms of urinary incontinence. Stress urinary incontinence (SUI) is the most common type. SUI is the complaint of involuntary leakage of urine with activity such as sneezing, coughing, or aerobic activity such as walking, running, etc. Urodynamic stress incontinence is the involuntary loss of urine from the urethra noted during a urodynamic study during increases in abdominal pressure, in the absence of a detrusor (bladder wall muscle) contraction or an over-distended bladder. Essentially, the abdominal pressure exceeds the resistance produced by the muscles surrounding the urethra or the resistance produced by the urethral closure mechanism. Two mechanisms for stress incontinence are well-recognized: *urethral hyper-mobility* or significant displacement of the urethra and bladder neck during exertion, and *intrinsic urethral sphincter deficiency (ISD)*. These mechanisms may coexist in certain cases.

Urethral hypermobility results from the loss of the normal pelvic support mechanism of the bladder. The bladder neck support is weakened, the increase in intra-abdominal pressure is no longer transmitted equally to the bladder outlet, and instantaneous leakage occurs. This may result from the trauma and stretching associated with vaginal delivery, hysterectomy, hormonal changes, pelvic denervation, or congenital weakness. Urethral hypermobility causes genuine SUI (GSUI) in most patients. The urinary sphincter is a muscle within the urinary system that allows the body to hold in urine. If the sphincter stops working, is paralyzed, or damaged, urine leakage may result, and this is known as intrinsic sphincter deficiency (ISD). It may result from prior operations, trauma, neurogenic changes, or atrophic changes. The goal of repairing SUI

from urethral hypermobility or ISD is to support the urethra and sphincteric unit. Symptoms of SUI include the sudden loss of urine during maneuvers that increase intra-abdominal pressure, such as coughing, laughing, sneezing, bending, straining, lifting, jumping, running, etc. SUI can be so severe often the patient will soak a pad or even require her to change her underpants or clothing.

Urinary urgency refers to a sudden, compelling desire to pass urine that is difficult to defer, or a strong need to pass urine for fear of leakage. Urge urinary incontinence commonly known as overactive bladder (OAB) is defined as involuntary leakage accompanied by (or immediately proceeded by) urgency. Patients with OAB will have a sudden desire to void (urgency). This may trigger urinary frequency, and if the patient is unable to reach the bathroom in time, she will have urge incontinence.

Mixed UI is a combination of SUI and OAB. Overflow incontinence occurs when the bladder doesn't completely empty. Dysfunctional nerves or urethra obstruction that impedes the flow of urine may cause overflow incontinence.

UI is diagnosed by history, physical examination, bladder log, questionnaires, and a pad test. Demonstration of urine loss per urethra on physical exam during an increase in intra-abdominal pressure is diagnostic of SUI. In more complicated cases, urodynamics and/or cystoscopy may be necessary to diagnose UI and to differentiate SUI from OAB. During the evaluation of UI, it is important to identify and determine the nature of the incontinence, the duration, the impact on quality of life and activities, prior treatments (medical, behavioral, and surgical) and predisposing and complicating factors. This will allow the practitioner to direct appropriate and effective treatment.

Urinary Incontinence can significantly impact a patient's physical and psychological quality of life. UI may lead to social isolation and withdrawal from an active lifestyle, resulting in weight gain and depression. Patients may withdraw from interaction with friends and family. Patients may be afraid to leave home or to participate in family events, religious services, or sporting activities. Intimacy is often adversely affected by UI. Hence the burden on women is significant, and this leads to a desire by patients and physicians to find effective, durable treatments to alleviate UI and allow the patient to return to an active lifestyle.

Urinary incontinence is an important medical problem for women in both the reproductive and menopausal phases of life. Urinary incontinence affects an estimated 15 to 50% of women, resulting in significant medical, social, and economic burden. Among women with incontinence, 50 to 80% are identified as having stress urinary incontinence or involuntary leakage of urine resulting from physical exertion or sneezing and coughing. By 2007 it was noted that, "an estimated 4 to 10% of women in the United

States undergo surgery intended to restore continence, and this rate has increased steadily during the past 20 years.[1]

III. TREATMENT OPTIONS FOR SUI

A. Behavioral and Non-Surgical Treatments

There are several non-surgical treatment options for SUI. In my experience, conservative treatment options are effective only in cases of mild SUI, and even then in only a minority of women. Conservative treatments include behavioral therapy or what is sometimes referred to as self-care, physical therapy, bio-feedback, electrical stimulation, devices, and medications. Behavioral modification or self-care includes weight loss, pelvic muscle exercises, smoking cessation, and timed voiding. Weight loss and smoking cessation can reduce the factors that aggravate incontinence. Pelvic floor exercises such as kegel exercises or vaginal weights can improve the strength of the pelvic floor to the bladder and urethra and improve mild urinary incontinence. Bio-feedback allows for sensors to be placed by the pelvic muscles to see which muscles are being used. This is designed to help recruit and strengthen the proper muscles in the pelvic floor responsible for continence. Electrical stimulation can stimulate and strengthen the pelvic muscles. External stimuli will make the muscles contract and assist in the strengthening of the appropriate muscles. A pessary is a device that comes in a variety of shapes and sizes and is placed in the vagina. Pessaries are used primarily for pelvic organ prolapse, but they also can be used as urethral support for treatment of incontinence. In my experience, they are often ineffective.

As it relates to medication, there is no FDA-approved pharmaceutical medication to treat SUI. Topical estrogen cream after menopause may contribute to a restoration of the vaginal wall and in some patients may improve continence to some extent.

Transurethral bulking agents may be injected to augment the urethral mucosal coaptation and seal effect to provide continence. The FDA has only approved bulking agents for SUI due to ISD. The success rate with bulking agents is often low and requires repetitive procedures; therefore, bulking agents have a limited role in the treatment of SUI. For more moderate to severe forms of SUI, non-surgical treatments have not been shown to provide favorable long-term results.[2]

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[1] Albo, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. N Engl J Med 2007;356:21.

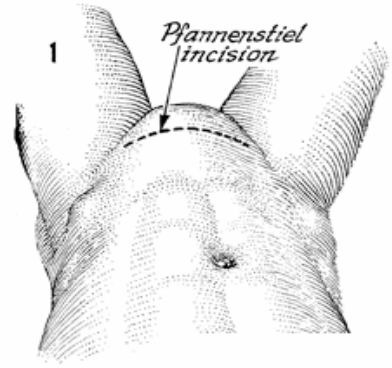
[2] Schiotz JA, Ten-year follow-up after conservative treatment of stress urinary incontinence. Int Urogynecol J 2008;19:911-915.

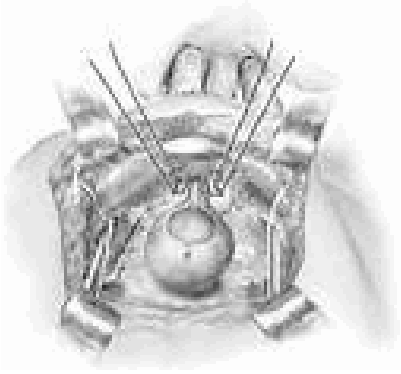
B. Traditional Surgical Options

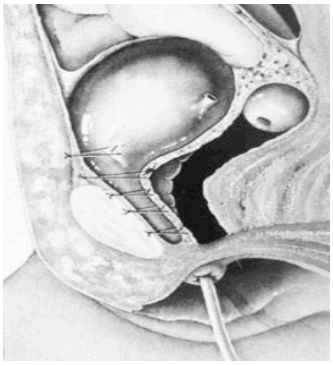
Prior to the development of mid-urethral slings, there was no one procedure that was the standard of care. Many different surgeons performed a variety of procedures in an attempt to correct SUI. These procedures included anterior plication, needle suspension, Marshall-Marchetti-Krantz (MMK), and open and laparoscopic Burch colposuspension. These procedures are considered native tissue repairs, but do require the use of a permanent suture such as Prolene or Gore-Tex. The pubovaginal facial sling is a sling procedure with native fascia and permanent sutures. I will address each of these procedures and its advantages and disadvantages.

Marshall-Marchetti-Krantz Procedure

The MMK procedure is also known as the retropubic suspension or bladder neck suspension surgery. The patient is placed under general anesthesia, and a long, thin, flexible tube (catheter) is inserted into the bladder through the narrow tube (urethra) that drains the body's urine. An incision is made in the lower abdomen, and the bladder is exposed. The bladder is separated from surrounding tissues. Permanent stitches (sutures) such as Prolene are placed in these tissues near the bladder neck and urethra. The urethra is then lifted, and the sutures are attached to the pubic bone itself, or to tissue (fascia) behind the pubic bone. The sutures support the bladder neck, helping the patient gain control over urine flow. In addition to general anesthesia, the MMK requires the patient to spend two-to-six days in the hospital. The MMK is not a procedure of choice today, as it leads to high bony complications and inferior long-term efficacy.[3]







Burch Procedure

The Burch procedure began being performed in the 1960s. Initially, this procedure was described by attaching the paravaginal fascia to the arcus tendineus. However, he

[3] Wu JY, Surgical therapies of female stress urinary incontinence: experience in 228 cases. Int Urogynecol J 2010;21:645-649; Chaliha C, Stanton SL, Complications of surgery for genuine stress incontinence. Br J Obstet Gynaecol. 1999 Dec;106(12):1238-45.

later changed the point of attachment to Cooper's ligaments because these were believed to provide more secure fixation points, and less chance of infection as seen with the prior MMK procedure. In the Burch colposuspension, permanent sutures such as Prolene are placed in the anterior vaginal wall at the level of the bladder neck and proximal urethra and are then sutured to the Cooper's ligament. The Burch returns the urethra to its anatomic location, which allows it to function more effectively in cases of GSUI. However, the Burch procedure is indicated only for GSUI, and is not a treatment for ISD, as success rates have been unacceptably low in this population. Since SUI due to ISD is often hard to detect, the Burch procedure fell out of favor with urologists. Also, the procedure requires an abdominal incision, is time-consuming, and requires a prolonged convalescence. Because of the significant post-operative morbidity, voiding difficulty, de novo pelvic organ prolapse, pain, and delayed failures, the Burch procedure has also lost popularity with surgeons.[4]

In two long-term studies, the effectiveness of Burch colposuspension has been shown to be time dependent, in that success rates have dropped significantly after 10 years. Further, pre-operative weight greater than 176 pounds has significantly affected cure rates. In the Kjolhede long-term study on Burch procedures, subjectively significant urinary incontinence was experienced by 56% of the patients.[5] In the Alcalay study, which suffered from more than 60% loss to follow-up, the Burch further demonstrated decline in cure rates, with only 19% of patients reporting no incontinence episodes.[6] The Burch procedure was also shown to have significant morbidity, urinary tract symptoms were experienced by 75% of patients, recurrent UTI in 4.6%, de novo detrusor instability in 14.7% of patients, long-term voiding difficulty in 22% of patients, and high rates of pelvic organ prolapse resulted from the Burch (37% in this study). Similar trends in a drop-off in efficacy have been documented at 2 or more years as reported by Demirci, along with late complications in 220 women including cystocele in 18, rectocele in 32, enterocele in 35, dyspareunia in 6, and groin or suprapubic pain in 15 patients.[7]

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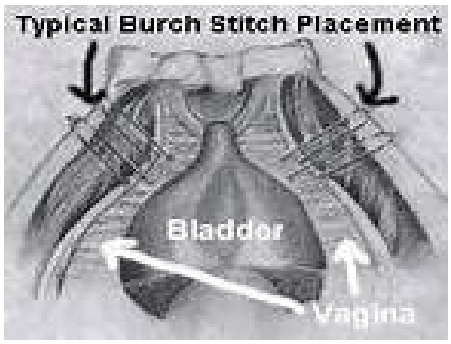
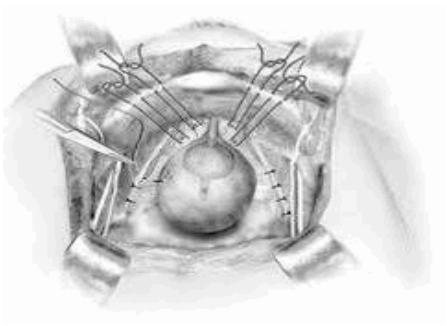
[4] Wu (2011): Trends in inpatient urinary incontinence surgery in the USA, 1998-2007; Nager (2012): A Randomized Trial of Urodynamic Testing before Stress-Incontinence Surgery; Chughtai (2013): Midurethral Sling Is the Dominant Procedure For Female Stress Urinary Incontinence: Analysis of Case Logs From Certifying American Urologists; Suskind (2013): Effectiveness of Mesh Compared with Nonmesh Sling Surgery in Medicare Beneficiaries; Rogo-Gupta (2013): Trends in the Surgical Management of Stress Urinary Incontinence Among Female Medicare Beneficiaries, 2002-2007; Wu (2014): The surgical trends and time-frame comparison of primary surgery for stress urinary incontinence, 2006-2010 vs 1997-2005: a population-based nation-wide follow-up descriptive study

[5] Kjolhede P, Long-term efficacy of Burch colposuspension: a 14-year follow-up study, Acta Obstet Gynecol Scand 2005, 84:767-772.

[6] Alcalay M, et al., Burch colposuspension: a 10-20 year follow-up, British Journal of Obstetrics and Gynaecology, Sept. 1995, Vol. 102, pp. 740-745.

[7] Demirci F, et al., Long-term results of Burch colposuspension. Gynecol Obstet Invest. 2001;51(4):243-7.





The decision to perform an open versus laparoscopic procedure depends on the skill set of the surgeon. Moehrer, et al., published a systematic review of laparoscopic colposuspension using the Cochrane Incontinence Review Groups' registry of randomized controlled trials, including four studies in the meta-analysis.[8] The meta-analysis demonstrated that subjective perception of cure was no different between the groups. When urodynamics were used to measure outcome, the success rate for the laparoscopic approach was significantly lower than that for the open procedure with an additional 9% risk of failure for laparoscopic versus open colposuspension. The laparoscopic procedure is not widely accepted by surgeons due to the steep learning curve required for laparoscopic suturing. It also requires abdominal entry and general anesthesia. The 2012 Cochrane Review by Lapitan concluded that there was not enough evidence to judge whether laparoscopic colposuspension has an advantage or disadvantage compared to the open Burch procedure in terms of subjective and objective cure rates, safety, longer-term complications, quality of life, and cost-effectiveness.[9]

The Ward Hilton study is a RCT of TVT versus Burch with 5-year follow-up. The TVT had similar efficacy and patient satisfaction and less voiding dysfunction.[10] Similarly, a Cochrane review of TVT versus Burch showed that TVT appeared to be as effective as open Burch colposuspension but with fewer complications, less voiding dysfunction, shorter operative times, and higher safety.[11] This benefit of TVT was also seen in Lapitan's 2012 Cochrane Review mentioned above. A meta-analysis by Novara found that patients receiving midurethral tapes, particularly TVT, had significantly higher overall (odds ratio [OR]: 0.61; confidence interval [CI]: 0.46–0.82; p = 0.00009) and

[8] Moehrer, B., Carey, M., Wilson, D., Laparoscopic colposuspension: a systematic review. BJOG. 2003;23(3):277-283.
[9] Lapitan MC, Cody JD. Open retropubic colposuspension for urinary incontinence in women. Cochrane Database Syst Rev. 2012 Jun 13.
[10] Ward, K., Hilton, P., Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up. BJOG 2008;115:226-233.
[11] Ogah, J., Cody, JD, Rogerson, L., Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD006375. DOI:10.1002/14651848.CD006375.pub2.

objective (OR: 0.38; CI: 0.25–0.57; $p < 0.0001$) cure rates than those receiving Burch colposuspension, although they had a higher risk of bladder perforation.[12]

Pubovaginal Sling Procedure

The pubovaginal sling procedure (PVS) places graft material directly under the urethra and attaches it to the connective tissue (fascia) of the abdominal muscles. The graft rests under the urethra like a firm hammock. When a cough or sneeze pushes the urethra down, it is forced against the sling, and the urethra is closed off. The sling procedure is often used for women who have had previous incontinence surgery. It also is recommended for women with a weakened urethral sphincter (ISD) that does not close properly. There are a number of materials that can be used to make the sling. Some doctors prefer to use a synthetic, nylon-like material, while others choose fascia—the strong tissue that surrounds muscle, removed either from the patient's abdomen (rectus fascia) or outer thigh (fascia lata) (autograft) or sterilized, irradiated fascia from a cadaver donor (allograft) or from an animal (xenograft).

The success rate of the sling is good, but long-term success rates may show some decline. In the SISTEr trial at seven years, the urinary continence rate (no reported leakage by the patient) was only 13% for the Burch procedure and 27% in the pubovaginal sling group.[13] However, both procedures showed decline in the long-term follow-up; 27% of patients required treatment for postoperative urge incontinence. In comparison to the Burch, the fascial sling has a higher rate of UTI, urge incontinence, voiding dysfunction, and the need for surgical revision to improve voiding. The increased efficacy but greater morbidity of the fascial sling is echoed in other systematic reviews and in my own practice and experience.[14]

One potential but relatively uncommon problem with this surgery is that the sling may compress the urethra and block the flow of urine, leading to urinary retention, incomplete bladder emptying, or de novo urgency. A major disadvantage of the autologous sling is the morbidity associated with fascial harvest including wound

[12] Novara G, et al., Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. Eur Urol 2010 Aug;58(2):218-38.

[13] Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries, Urology 2012;188:485-489; Albo, ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155.

[14] Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries, Urology 2012;188:485-489; Albo ME, et al., Burch colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155; Brubaker L, 5-Year Continence Rates, Satisfaction and Adverse Events of Burch Urethropexy and Fascial Sling Surgery for Urinary Incontinence, Urology 2012;187:1324-1330; Rehman H, et al. Traditional suburethral sling operations for urinary incontinence in women. Cochrane Database Syst Rev. 2011 Jan 19.

complications, infection, pain, nerve entrapment and necessity of an additional surgical site if fascia lata is obtained with attendant complications and decreased mobility, and the associated hospital stay and convalescence of the procedure. Allografts and xenografts avoid the abdominal incision and the morbidity of fascial harvest, but can be associated with rejection, disease transmission, and expense. There are also occasional religious and cultural objections from patients with respect to donor and xenograft tissue. Moreover, allografts and xenografts do not have the long-term durability of synthetic material. They have been shown to degrade and decompose in patients on follow up.

It is my opinion that anterior plications, needle suspension (such as the Raz procedure), paravaginal defect repair, and the MMK should not be offered as treatment options for SUI. The success rates are unacceptably low and the benefits do not outweigh the risks. My opinion is in agreement with the 2013 National Institute for Health and Care Excellence (NICE) guidance.[15]

Today, the traditional operations have been in part replaced in general practice by retropubic or transobturator midurethral synthetic slings, which includes the TVT, TVT-O, and TVT Abbrevo. TVT, TVT-O, and TVT Abbrevo are synthetic mid-urethral slings which are used by more than 95% of pelvic floor surgeons. The literature, conversations with colleagues, and my experience show that most pelvic floor surgeons prefer TVT to the traditional procedures, with the exception of a few select circumstances. Additionally, native tissue procedures are rarely taught in medical school or residency.[16]

IV. TVT AND THE MIDURETHRAL SLING

A. TVT History and Clinical Results

The Gynecare TVT mesh is made from a polypropylene mesh, more specifically the Prolene mesh. Polypropylene mesh has been used as a permanent human implant for decades. The first polypropylene meshes were developed and used by hernia surgeons in the 1950s. In the early 1970s, Ethicon developed Prolene mesh for hernia surgery. The Prolene mesh was made from the same material in Prolene sutures (polypropylene and certain extracts), which had been used since the 1960s as well. The Prolene sutures have been used for cardiovascular repairs, plastic surgery, hernia repairs, and pelvic floor repairs. Before it was used for treatment of SUI, the inflammatory response and appropriateness of Prolene in the body was widely known.

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[15] National Institute for Health and Care Excellence, Urinary incontinence: The management of urinary incontinence in women, Sept. 2013 at guidance.nice.org.uk/cg171.

[16] Nager CW, et al., A Randomized Trial of Urodynamic Testing before Stress-Incontinence Surgery. N Engl J Med 366;21:1987–1997; Clemons JL, et al., Impact of the 2011 FDA Transvaginal Mesh Safety Update on AUGS Members' Use of Synthetic Mesh and Biologic Grafts in Pelvic Reconstructive Surgery. Female Pelvic Med Reconstr Surg 2013;19:191-198, Chughtai BI, et al., Midurethral Sling Is the Dominant Procedure for Female Stress Urinary Incontinence: Analysis of Case Logs From Certifying American Urologists. Urology 2013.

In the early 1990s, Dr. Ulmsten, a physician in Sweden, was working on a new way to treat SUI. At the time, there was no standard, widely accepted method of repair; therefore, surgeons were using a variety of methods. All of the methods at the time had high recurrence rates, significant morbidity, substantial complications, long hospital stays, and substantial recovery times.

In the 1980s to mid-1990s, Dr. Ulmsten and Dr. Petros began to use several different types of meshes and placed them under the mid-urethra.[17] They found that the Prolene mesh had the best results. Dr. Ulmsten was seeking to determine if the support was more appropriate at the bladder neck or if it was in the mid-urethral section, which was a newer concept. After years of research, he established the integral theory, and began placing meshes in the mid-urethra tension-free—that is, not chronically kinking the urethra as was done with the Burch, MMK, and other procedures.[18]

As Dr. Ulmsten determined the location of the mesh, he was also assessing the appropriate tools and size of the tools to place the mesh. He determined that a retropubic pass with 6 mm needle would be appropriate, as it was large enough to palpate to allow safe passage without causing significant effect on the surrounding tissue.

Dr. Ulmsten then had to determine what type of mesh would be left behind that would integrate well, not cause infections, provide the appropriate support, but also adapt to the stresses in the body. Dr. Ulmsten used the meshes that were available on the market such as Mersilene, Gore-Tex, Marlex, Prolene, and others. He found that the Prolene mesh provided the key qualities needed for a permanent mesh for incontinence repair. Prolene was not rejected by the body, did not cause defective healing, provided the appropriate support, and significantly improved both subjective and objective cure and comfort rates. Then it had to be determined what size mesh would be used. Dr. Ulmsten determined that a 1 centimeter wide and 40 centimeter long Prolene Mesh would work best. The mid-urethral complex (continence zone) measures 1 cm in length, hence the TVT mesh is able to support the entire mid-urethra. The length of the mesh was moved to 45 cm to allow treatment of even obese women and the width to 1.1 cm. The actual length of the mesh that is implanted averages 15 cm (range 12-30).

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[17] Petros PE, Ulmsten UI, An integral theory and its method for the diagnosis and management of female urinary incontinence. Scand J Urol Nephrol Suppl. 1993;153:1-93; Ulmsten U, et al., A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1998;9(4):210-3; Petros P., Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J 2015 Apr;26(4):471-6.

[18] Ulmsten U, et al., An Ambulatory Surgical Procedure Under Local Anesthesia for Treatment of Female Urinary Incontinence, Int Urogynecol J (1996) 7:81-86; Ulf Ulmsten, Intravaginal Slingplasty (IVS): An ambulatory surgical procedure for treatment of female urinary incontinence. Scand J Urol Nephrol 1995;29:75-82.

The Prolene Mesh also has strong adhesive (friction) properties that makes suture fixation unnecessary. A plastic sheath surrounds the TVT mesh and facilitates placement of the sling into the correct position below the urethra. The plastic sheath also prevents contamination at the time of sling placement. Hence the design of the instrument and the surgical technique enabled the sling not only to be located in a correct anatomical position, but also to be firmly secured immediately. The friction prevents sliding of the mesh that can result in loosening and a failed operation.

By 1996, Dr. Ulmsten completed his first trial, which included 75 patients with two-year follow-up. 92% of the patients were cured or significantly improved, with no tape rejection, no defective healing, no intra-operative complications and no post-operative complications.[19]

During the mid-1990s, Ethicon began discussing with Dr. Ulmsten his approach to correct SUI. Dr. Arnaud went to visit Dr. Ulmsten and had an opportunity to watch multiple surgeries and to speak with the patients. Dr. Arnaud brought in outside physicians who specialized in urinary incontinence repair to view the procedure. Based upon seeing the procedure and the clinical results, Ethicon determined that this procedure could change the way SUI repair was performed and could be a significant benefit to patients.[20]

In 1997, Ethicon began to sell TVT in Europe. In 1998, a prospective randomized study with six centers was carried out in Scandinavia and tested the safety and efficacy of the TVT device. A compilation of the data that was published in 1998 showed 91% cure rates, with another 7% significantly improved.[21] The results demonstrated the procedure was safe, effective, and less invasive than prior anti-incontinence procedures. There was a clear benefit to patients that no other procedure was providing.

The results of the trial were about the same as those reported by Dr. Ulmsten. That is, less-experienced surgeons were able to replicate the continence outcomes of experienced surgeons without compromising patient safety. This was attributed to the unique design of the mesh and the use of a specific trocar to place the mesh. Furthermore, the TVT procedure could be performed as an outpatient procedure, with less peri-operative morbidity and convalescence when compared to prior SUI procedures such as the Burch, MMK, or Pubovaginal Sling. With the tremendous results from these clinical trials and others, as well as the wide acceptance in Europe, Ethicon began to sell the TVT in the United States in 1998.

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[19] Ulmsten U, et al., An Ambulatory Surgical Procedure Under Local Anesthesia for Treatment of Female Urinary Incontinence. Int Urogynecol J 1996;7:81-86.
[20] History of TVT, ETH.MESH.03932912-03932914.
[21] Ulmsten U, A Multicenter Study of Tension-Free Vagina Tape (TVT) for Surgical Treatment of Stress Urinary Incontinence. Int Urogynecol J 1998;9:210-213.

Considering how prevalent SUI is in the female population, it is not possible for all women with this condition to be treated by specialists. Rather, it is important that a procedure can be performed by a wide-variety of urologists and gynecologists who practice in various communities. It is unrealistic to expect that all women with SUI can be treated at tertiary care centers in metropolitan areas. As a result of its success and relative ease of use, the minimally invasive mid-urethral sling has been widely adopted, and is successfully used throughout the world in the surgical treatment of stress urinary incontinence. The ability of many surgeons to obtain great results was demonstrated in a study where over 7,000 Medicare patients were assessed, with 93.8% receiving a mesh repair with superior results compared to non-mesh repairs.[22] This was also demonstrated in hundreds of studies, systematic reviews, and meta-analyses. This is why tension-free mid-urethral slings have become the gold standard for treatment of SUI.

The Prolene mesh Dr. Ulmsten used in his first studies was the same mesh that Ethicon has used in the TVT, with the exception that a blue dye was added and, beginning in 2006, TVT offered a laser-cut or mechanical-cut mesh.[23] I have used both mechanical-cut and laser-cut mesh, and clinically there is no difference between the two. This is further confirmed in the literature. The earlier literature discussing complication rates and success rates with the TVT are the same for the more recent literature when laser-cut mesh is made. This makes sense because there is simply a change in the method of cutting the mesh. Any difference in the stiffness of the two types of mesh is not clinically significant. Prestretching the mesh to 50% elongation and bench testing without the sheath and trocars is not how one actually uses the TVT mesh in the operating suite.

In 2006, Ethicon used a study by Long Lin to determine the forces on the mesh.[24] Those forces were applied and the mesh was tested for flexural rigidity and elongation, and there were no significant differences. This was performed because some physicians were concerned that there were mesh particles, known as fraying, coming from the mechanically cut mesh. The overall clinical literature and my experience do not show that any particles of the Prolene polypropylene have a clinical effect in patients. The literature shows that clinically the TVT mesh is well-tolerated by patients.

In short, both mechanical and laser-cut TVT meshes are appropriate for use in the body, and are both safe and efficacious as demonstrated by the literature and as evidenced in my practice.

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[22] Suskind AM, et al., Effectiveness of Mesh Compared With Nonmesh Sling Surgery in Medicare Beneficiaries. Obstet Gynecol 2013;0:107.

[23] ETH.MESH.9275943-45.

[24] Tong A, Lin L, et al., In Vivo tension sustained by Fascial Sling in Pubovaginal Sling Surgery for Female Stress urinary Incontinence. Urol 2005; ETH.MESH.01784823-28 (CER Laser Cut Mesh); ETH.MESH.01222075-79 (Elongation Characteristics of Laser Cut Prolene Mesh for TVT); ETH.MESH.06696367-79 (Performance Evaluation of TVT U Prolene Mesh).

The mesh in TVT was and is state of the art and the most commonly used mesh for stress urinary incontinence. It is a Type 1 macroporous monofilament mesh that has shown the best tolerability for use in stress urinary incontinence in its 1.1 cm size and configuration. Among the SUI meshes, it has the largest pore size, which is clearly over 1 millimeter, even assessed, as I have done, by putting the mesh next to a millimeter ruler. The Cochrane Review by Ogah found that TVT has better efficacy and lower erosion rates than multifilament non-Type 1 meshes.[25] Falconer also found minimal inflammation with the Prolene mesh and practically no tissue reaction even out to two years, while there was no difference between paraurethral connective tissue in biopsies from patients operated on with Prolene tape and in controls two years after surgery.[26] The TVT mesh has the optimal weight for long lasting continence and tolerability, as shown by the numerous long-term studies discussed in my report.

More than 80 randomized controlled trials have assessed the TVT and approximately 1,000 studies have addressed the TVT mesh.[27] Put simply, it is the most studied SUI device ever sold, and more data is available for the TVT device than for any other SUI treatment. Every major professional medical society that serves the needs of women with SUI has endorsed the TVT (as well as a few similar MUS) as being the standard of care for treatment of SUI.

The American Urogynecologic Society (AUGS) is the largest professional society representing the medical specialty of urogyencology. The AUGS consists of more than 1,500 physicians. The AUGS has adopted a position statement that full-length mid-urethral slings such as the TVT (both retropubic and transobturator) have been extensively studied, and are safe and effective relative to other treatment options. The TVT remains the leading treatment option and current gold standard of care for stress incontinence surgery. This most-highly-respected organization has determined the standard of care today is the TVT and similar mid-urethral slings. In other words, women with SUI that have failed non-surgical options are offered the TVT, unless there are significant patient factors prohibiting such.[28]

The American Urological Association (AUA) is the largest professional organization for urologists. The AUA has also provided a position statement on the use of transvaginal mesh for the surgical treatment of SUI. "*Suburethral synthetic*

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[25] Ogah J, Cody DJ, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn. 2011 Mar;30(3):284-91.

[26] Falconer C, et al. Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. Int Urogynecol J Pelvic Floor Dysfunct. 2001;12 Suppl 2:S19-23.

[27] A Systematic review of patient-years of experience in prospective randomized controlled trials (RCTS) in incontinence, ETH.MESH 07246690-719; CER TVT Family of Products, ETH.MESH.10178882-10179216.

[28] Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders, American Urogynecologic Society, 2013.

polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries."[29] The AUA believes the data uniformly and overwhelmingly supports the use of mid-urethral slings (TVT) for the treatment of SUI, and as a result, it is the most commonly used procedure. As a long-term AUA member, I fully agree with and endorse this position statement, which echoes my own medical opinion.

The National Institute of Health and Care Excellence (NICE) in the United Kingdom has published 2013 guidelines for The Management of Urinary Incontinence in Women. NICE states that "When offering a synthetic mid-urethral tape procedure, physicians are only to use procedures and devices for which there is current high quality evidence on efficacy and safety." NICE then defines five procedures as meeting this standard, including TVT. NICE further states that devices for SUI should use Type 1 macroporous polypropylene tape. Type 1 mesh, as defined by the Amid classification, includes TVT mesh.

It is interesting that plaintiffs' experts would contradict the NICE statement and claim that Prolene mesh in TVT is not Type 1, and therefore inappropriate for SUI surgery. These opinions are clearly contrary to the current medical literature and accepted medical practice. TVT mesh is macroporous (Amid, >75 microns). TVT mesh has a pore size of more than 1,300 microns, and is among the largest-pore-size SUI mesh. TVT mesh is also lightweight (100 g/m^2) for SUI application. The mesh is only 1.1 cm wide. It has the greatest elasticity when compared to similar products. The TVT mesh's pore size is 18 times larger than the pore size required to be considered macroporous mesh. Most reasonable surgeons would agree that TVT is the prototypical lightweight Type 1 mesh in the SUI application that has been copied by multiple manufacturers around the world.

Plaintiffs' experts have made unsubstantiated claims that Dr. Ulmsten's data may be tainted with bias, and that his long-term data cannot be relied upon. However, Dr. Ulmsten's data has been widely accepted by the medical community of physicians who treat SUI. Dr. Ulmsten's early studies in 1998 were assessing not only his center, but also five other centers. If Dr. Ulmsten was getting good results but the others were not, statistically you could not have an overall 90% success rate with no mesh rejection or serious complications. Unfortunately, Dr. Ulmsten is unable to defend himself, as he is deceased. The opinions of plaintiffs' experts are contrary to the opinions expressed by multiple major medical professional societies and the peer reviewers of numerous publications. Nonetheless, the findings of his studies have been replicated time and time again by other surgeons and centers and these results have been published in virtually every medical journal concerning urinary incontinence. The efficacy and safety of the TVT has also been assessed and acknowledged by numerous Cochrane Reviews by Ford,

[29] AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence, 2011.

Ogah, and Lapitan, the AUA in its SUI Guidelines, the SGS in its systematic review and recommendations, and the EUA in its SUI Guidelines.

Dr. Ulmsten's 17-year data was recently published by Dr. Nilsson.[30] The study showed that there was a 91.3% objective cure rate, no clinically significant contracture, no tape rejection and one mesh exposure, which was asymptomatic and due to vaginal atrophy in the elderly patient who was satisfied. This study demonstrated the TVT is safe and effective after 17 years.

In 2010, Dr. Olsson, et al., also published the clinical results of 11.5 years of follow-up with the TVT procedure. In this study, 147 women were assessed. The objective cure rate was 84%, with 95% of patients being subjectively cured or improved. Of note, bladder perforations were 2.7%, urethral injury 1.4%, and urinary infection was 7.2%. There was one healing defect at two months post-op and no late tape rejection. At follow-up, none of the patients had voiding difficulties. The authors' conclusion was that the procedure was safe and effective after more than 10 years.[31]

Dr. Serati, et al., published another long-term study on TVT in 2012. This group studied patients for 10 years, and the first sentence of his report says it all—the TVT is one of the most effective surgical treatments for SUI. The 10-year subjective, objective, and urodynamic cure rates were 89.7%, 93.1%, and 91.4% respectively. Ten years after surgery, no significant deterioration of either subjective or objective outcomes was observed. As it related to complications, bladder perforations occurred in 3.8% of the cases. In both situations, the bladder lesion was identified during the operation, and the tape was promptly removed and replaced. No severe bleeding or other intraoperative complications occurred. No postoperative complications requiring surgical intervention occurred. Voiding difficulties were reported in two patients. No patient required tape release or resection during the 10-year follow-up. No significant POP, vaginal, bladder, or urethral erosion, or de novo dyspareunia were noted in the remaining 58 patients.[32] TVT consistently shows in many long-term trials that it is safe and effective, and is the standard of care for SUI.[33]

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[30] Nilsson CJ, Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J, 2013.

[31] Olsson I, et al., Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence. Int Urogynecol J 2010;21:679-683.

[32] Serati M, Tension-free Vaginal Tape for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 10-Year Follow-Up. Eur Urol 2012;61:939-946.

[33] Laurikainen E, et al., Five-year results of a randomized trial comparing retropubic and transobturator midurethral slings for stress incontinence. Eur Urol. 2014 Jun;65(6):1109-14; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J 2013 Aug;24(8):1271-8; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol 2012 Nov;19(11):1003-9; Aigmueller T, et al., Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol 2011 Nov;205(5):496.e1-5; Bjelic-Radisic V, Patient related outcomes and Urinary Continence Five Years

SUI, as stated above, affects patients' sexual dysfunction. Sutherst and Brown found that 43% of patients felt their urinary disorder adversely affected sexual relations.[34] TVT has demonstrated good results as it relates to sexual function after TVT is implanted.[35] In the Shah study, there was no negative effect on sexual function with the TVT.[36] In another study, only 3.8% reported intercourse to be worse after TVT. In Maaita, when sexual function was again assessed, there was no dyspareunia and the conclusion was that "patients can be reassured that this operation [TVT] will not affect their sex life."[37] In my practice, it is uncommon for the TVT to adversely affect a patient's sexual function, and very rare to have pain with intercourse as related to the TVT. Traditional procedures such as the Burch can also adversely affect sexual function. In a study, by Zimmern and Lemack after the Burch was used, 20% of patients reported intercourse to be worse.[38]

TVT has further shown good results in obese patients. Most studies have shown there is no significant difference in success rates depending on BMI index.[39] TVT has also shown very good results in women with pure ISD.[40]

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after the Tension-Free Vaginal Tape Operation. Neurourology and Urodynamics 2011;30:1512-1517; Wu J, Surgical therapies of female stress urinary incontinence: experience in 228 cases. Int Urogynecol J 2010;21:645-649; Hil Song P, The 7-year outcome of the tension-free vaginal tape procedure for treating female stress urinary incontinence. 2009 BJU Int, 104, 1113-1117; Christian J, et al., Long-term outcomes of TVT and IVS operations for treatment of female stress urinary incontinence: monofilament vs. multifilament polypropylene tape. Int Urogynecol J 2009;20:703-709; Celebi I, Results of the tension-free vaginal tape procedure for treatment of female stress urinary incontinence: a 5 year follow-up, Arch Gynecol Obstet 2009;279:463-467; Liapis A, Long-term efficacy of tension-free vaginal tape in the management of stress urinary incontinence in women: efficacy at 5 and 7 year follow-up. Int Urogynecol J 2008;19:1509-1512; Jelovsek JE, et al, Randomized trial of laparoscopic Burch colpususpension versus tension-free vaginal tape: long-term follow up. BJOG 2008;115:219-225; McCracken GR, Five Year Follow-up Comparing Tension-Free Vaginal Tape and Colposuspension. Ulster Med J 2007;76 (3) 146-149; Chene G, Long-term results of tension-free vaginal tape (TVT) for the treatment of female urinary stress incontinence. European Journal of Obstetrics and Gynecology and Reproductive Biology, 2007;134:87-94; Kuuva N, et al., Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women. Acta Obstetricia et Gynecologica 2006;85:482-487.

[34] Sutherst J, Sexual dysfunction associated with Urinary Incontinence. Urol Int 1980; 35:414-416.

[35] Jha S, Impact of Incontinence Surgery on Sexual Function: A Systematic Review and Meta-Analysis. J Sex Med 2012;9:34-43.

[36] Shah SM, et al., Impact of Vaginal Surgery for Stress Urinary Incontinence on Female Sexual Function: Is the Use of Polypropylene Mesh Detrimental, Urology 2005.

[37] Maaita M, et al., Sexual function after using tension-free vaginal tape for the surgical treatment of genuine stress incontinence. BJU Intl 2002;90, 540-543.

[38] Lemack, et al., Sexual function after vaginal surgery for stress incontinence: results of a mailed questionnaire. Urol 56:223-227, 2000.

[39] Greer WJ, Obesity and Pelvic Floor Disorders: A Review of Literature, Obstet Gynecol, 2008 August, 112 (2 Pt 1): 341-349; Osborn DJ, Obesity and Female Stress Urinary Incontinence, Urology 2013;82:759-763, 2013; Revicky V, et al., Obesity and the Incidence of Bladder Injury and Urinary Retention Following Tension-Free Vaginal Tape Procedure: Retrospective Cohort Study, Obstet and Gynecol Int 2011.

Advantages of TVT include shorter operative time, lower anesthetic requirement, reduced peri-operative morbidity, reduced surgical pain, reduced hospitalization, reduced convalescence, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low.[41]

Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries, but are known to occur with non-mesh sling procedures as well. It is the AUA's opinion that any restriction of the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI: "Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5-10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of follow-up." Based on this data, the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques. This is consistent with my medical opinion and experience, and with the medical literature. This systematic review and meta-analysis also found lower rates of pain and sexual dysfunction with the midurethral sling as compared to the Burch and autologous sling without bone anchors. The SGS systematic review and meta-analysis also found lower rates of dyspareunia with the retropubic TVT compared to the Burch and pubovaginal sling.[42]

A 2014 systematic review and metaanalysis found that retropubic midurethral slings had more favorable objective and subjective cure rates than transobturator midurethral slings, but not significantly so.[43] A 2015 systematic review and metaanalysis, on the other hand, found similar objective cure rates between retropubic and

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[40] Ghezzi F, Tension-free vaginal tape for the treatment of urodynamic stress incontinence with intrinsic sphincteric deficiency, Int. Urogynecol J 2006;17:335-339; Rezapour M, Tension-Free Vaginal Tape (TVT) in Stress Incontinent Women with Intrinsic Sphincter Deficiency (ISD)-A Long Term Follow-up, Int. Urogynecol J 2001;(Suppl 2):S12-S14; Bai S, Treatment outcome of tension-free vaginal tape in stress urinary incontinence: comparison of intrinsic sphincter deficiency and nonintrinsic sphincter deficiency patients, Int. Urogynecol J 2007;18:1431-1434; Choo G, et al., Long-term Outcomes of Tension-free Vaginal Tape Procedure for Treatment of Female Stress Urinary Incontinence with Intrinsic Sphincter Deficiency, Int Neurourol J 2012;16:47-50; De Souza A, Sexual function following retropubic TVT and transobturator Monarc sling in women with intrinsic sphincter deficiency: a multicenter prospective study, Int Urogynecol J 2012;23:153-158.

[41] Aigmueller T, et al., Reasons for dissatisfaction ten years after TVT procedure. Int Urogynecol J 2014;25:213-217.

[42] Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.

[43] Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.

transobturator midurethral slings, but higher subjective cure rates in retropubic slings.[44] A long-term study published in 2014 comparing retropubic and transobturator slings found comparable objective and subjective cure rates between the two devices with low complication rates.[45]

In summary, 17 years ago when surgery was recommended for patients who had bothersome stress urinary incontinence (SUI), they were offered operations such as suburethral (Kelly) plication, needle urethropexy, open or laparoscopic Burch procedure, and pubovaginal fascial sling procedure. Today, the overwhelming majority of operations for SUI have been replaced in general practice by retropubic or transobturator midurethral synthetic slings, which includes the TVT and TVT-O. It has been reported that there have been more than 3 million mesh slings sold since the mid-1990s. The TVT mid-urethral slings have been studied more than any other incontinence surgery and are safe and effective.[46] The Burch and the PVS are more invasive and have greater peri-operative morbidity than midurethral slings. They cause more voiding dysfunction and have significantly greater convalescence, making them less attractive for most primary cases of SUI. These procedures are generally reserved for patients with risk factors for mesh implantation and those that have failed TVT. In fact, many of the traditional procedures for SUI such as the Burch colposuspension and the pubovaginal sling procedure are rarely performed and few Urologists, Gynecologists, or Urogynecologists are proficient at these procedures.[47]

B. Benefits of TVT

Stress urinary incontinence is a symptom of urine loss due to events that result in increased abdominal pressure such as sneezing, coughing, physical exercise, lifting, bending, or even changing positions. Approximately 50% of all women experience SUI and seek treatment. Surgery to treat SUI is discussed in women who have failed non-operative measures. The AUA defines the index patient with SUI as an otherwise healthy woman who has elected surgical therapy for the correction of SUI. Placement of sub-

[44] Tommaselli GA, et al., Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015.
[45] Laurikainen E, Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014;
[46] Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27; Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375. DOI: 10.1002/14651858.CD006375.pub3.
[47] Walters MD, Which Sling for which SUI patient?, OBG Management, Vol. 24 No. 5, May 2012; Clemons JL, et al., Impact of the 2011 FDA transvaginal mesh safety update on AUGS members' use of synthetic mesh and biologic grafts in pelvic reconstructive surgery. Female Pelvic Med Reconstr Surg 2013 Jul-Aug;19(4):191-8. doi: 10.1097/SPV.0b013e31829099c1; Chughtai BI, et al., Midurethral sling is the dominant procedure for female stress urinary incontinence: analysis of case logs from certifying American Urologists. Urol 2013 Dec;82(6):1267-71.

urethral synthetic polypropylene mesh slings such as the TVT is the most common surgery performed for SUI.

Extensive data exist to support the use of synthetic polypropylene mesh sub-urethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries such as Burch, MMK, or PVS. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction, higher long-term success rates, and low complications. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low in the index patient and the rate of reoperation for voiding dysfunction and exposure has been consistently reported to be around 2-5% out to a decade or more in the various studies, metaanalyses, and database reviews.[48] Surgery due to pain is less than 1% per these data. Additionally, it is important to note that most sling-related complications such as urinary retention, UTI and pelvic pain are not unique to transvaginal mesh, and can occur with non-mesh sling procedures as well.

In 2015, a Cochrane review of midurethral sling (MUS) operations for SUI in women was published. The review noted that the MUS, a word that is often used interchangeably with TVT, is the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and has a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. Midurethral slings have a positive impact on improving the quality of life of women with SUI. When comparing retropubic techniques, the bottom-to-top route was more effective than top-to-bottom route.[49]

A 2013 article in *Nature* stated that the "traditional gold standards of Burch retropubic colposuspension and pubovaginal slings are still appropriate treatment options for some patients, but randomized controlled trials have demonstrated that synthetic midurethral slings are just as effective as these traditional procedures but with less associated morbidity.[50] Thus, midurethral slings—inserted via a retropubic or transobturator approach—have become the new gold standard first-line surgical treatment for women with uncomplicated SUI. Pubovaginal slings remain an effective option for women with SUI who have failed other procedures, have had mesh complications, or who require concomitant urethral surgery. Based on the literature a new gold standard

[48] Welk et al JAMA Surg 2015; Unger et al IUJ 2015; Schimpf et al, 2014; Laurikainen et al 2014; Jonsson Funk et al, 2013; Svenningsen et al, 2013; Nguyen et al, 2012; Ogah et al, 2009; Novara et al 2008.

[49] Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375. DOI: 10.1002/14651858.CD006375.pub3.

[50] Cox A, Herschorn S, Lee L, Surgical management of female SUI: is there a gold standard? Nature 2013;10:78-89.

first-line surgical treatment for women with SUI is the synthetic midurethral sling inserted through a retropubic or transobturator approach."[51]

Based on this data, the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques.[52] The 2012 Update reconfirms these results and shows that TVT has lower adverse events like pain and sexual dysfunction, less voiding dysfunction, similar bladder injury as Burch, and is less invasive, with decreased morbidity and limitations.

The Ethicon TVT mesh has favorable biomechanical properties. I have used both mechanically-cut and laser-cut mesh, and in my opinion, both products are safe and effective. I feel comfortable implanting the TVT mesh, as it has over 17 years of data to support its use in women with SUI. This efficacy is equivalent or superior to other surgical techniques.

There is no difference in laser-cut versus mechanically cut mesh. Data shows they perform the same. The data from 1998 to 2006 (before laser-cut mesh was available) is consistent with the data from 2006 to the present (when laser-cut mesh was available), showing similar efficacy and safety in hundreds of studies, RCTs, and reviews. The data show no difference in exposures over time. Clinically they are the same. In the physiologic range, there is similar and equivalent distensibility. The available medical literature does not show any distinction between mechanically cut mesh and laser-cut mesh. Contrary to the testimony by plaintiffs' experts, there was no statistically significant difference in exposure rates. In the Hinoul 2011 study, it was noted that post-op pain and recovery were quicker with the laser-cut TVT Secur. In a single-center randomized clinical trial, after a 3-year minimum follow-up, the TVT-Abbrevo (laser-cut mesh) procedure with a shorter tape and reduced dissection was found to be as safe and efficient as the TVT-O procedure (mechanical-cut mesh) for treating female SUI, with less severe and frequent groin pain in the immediate postoperative period.[53] Similarly, Tomaselli showed that both TVT-Abbrevo and TVT-Obturator are effective and safe for

[51] Cox A, Herschorn S, Lee L, Surgical management of female SUI: is there a gold standard? Nature 2013;10:78-89.
[52] Dmochowski RR, Update of AUA Guideline on the Surgical Management of Female Stress Urinary Incontinence. Urology 2010;183:1906-1914.
[53] Waltregny D and de Leval J, New Surgical Technique for Treatment of Stress Urinary Incontinence TVT-Abbrevo: From Development to Clinical Experience. Gynecology – Surgical Technology International XXII 2012:1-9.

the surgical management of SUI.[54] TVT-Abbrevo is associated with less post-operative pain. Other data do not show a difference in exposure rates.

The TVT device is truly a transformational device in SUI surgery for two reasons:

(1) The location of the sling at the mid-urethra rather than the bladder neck. Sling location at the mid-urethra has allowed a more straightforward dissection and less urethral obstruction;

(2) Placement of the sling in a "tension-free" manner (that is, not using any sutures or bone-anchor to set the sling in a fixed location). The sling is placed loosely, without elevation of the urethra. This device was designed to allow a procedure that could be replicated by a wide variety of surgeons throughout the world. Dr. Ulmsten's concept of a loosely applied sling at the mid-urethra resulted in less urethral obstruction without compromising efficacy. It is also revolutionary in that it is an effective SUI treatment out to long term, while minimally invasive compared to Burch and pubovaginal slings.

I have been using both the TVT Obturator since 2004 and Retropubic kits since 1999. I have performed more than 500 TVT procedures. I have an 85-90% success rate and less than a 2% complication rate. These complications include 0.5% perforation rate to the bladder or urethra and a 1.5% incidence of mesh exposure. In patients with mesh exposure, some may be treated with estrogen creams. Others may need a partial mesh excision to resolve the mesh-related complication.[55]

I am aware of the Public Health Notifications in regards to transvaginal mesh. These notifications initially included prolapse mesh and mesh slings. The second notification, however, excluded meshes for SUI, which was the correct decision. The FDA in 2013 published the update on SUI slings and found that the TVT was safe and effective, as had been done in 2011 by the FDA Advisory Panel. Further, despite legal issues pertaining to transvaginal mesh, the TVT procedure remains an integral component of my practice as well as the practices of most pelvic surgeons. I feel confident recommending this product to women in my practice, or to a friend or a family member. I have personally performed the TVT procedure on women from 18 to 88 years of age. I have personally witnessed the dramatic return of my patients to active lifestyles, with significant improvement in their quality of life.

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[54] Tommaselli GA, et al., Comparison of TVT-O and TVT-Abbrevo for the Surgical Management of Female Stress Urinary Incontinence: a 12-Months Preliminary Study. Intl J of Gynecol & Obstet 2012 (Abs. 0692).

[55] Shah K, et al., Surgical management of lower urinary mesh perforation after mid-urethral polypropylene mesh sling: mesh excision, urinary tract reconstruction and concomitant pubovaginal slings with autologous rectus fascia. Int Urogynecol J 2013.

Because I practice in a tertiary care center and I am a national expert in SUI surgery, I see a disproportionate number of women with complex SUI (failed surgery, neurogenic dysfunction, fistula) that may not be appropriate for the TVT. I use biological graft material in 50% of cases. This case distribution would be different if I worked in a community practice. For example, 53% of AUGS members reported that before the 2011 FDA warning, 99% of the responding members used synthetic mesh slings. After the FDA statement, respondents reported an overall decrease in the percent of mesh used in POP cases, but no change in synthetic mesh sling use.[56] Physicians who treat SUI should be well-versed in a wide variety of treatments for SUI, and should individualize the treatment based on what is best for that particular patient.

I agree with the AUA that patients should be counseled regarding the surgical and nonsurgical options, including benefits and risks. Choice of the procedure should be a collaborative decision between the surgeon and patient, and should consider patient preferences as well as surgeon experience and judgment. The decision to use mesh should be based on the judgment of the surgeon and made in the best interests of the patient. After a thorough discussion with the index patient with SUI, I enthusiastically recommend the TVT to most of the patients in my practice with SUI that failed non-operative measures. I make this recommendation based on the high success rate demonstrated in more than a thousand studies in the peer-reviewed literature. Even though the Burch and pubovaginal sling have been around for decades more than the TVT, the data on them is more limited and lacking, as noted in the first systematic review performed back in 1996 by Black and Downs, who concluded that the data were very poor to the effect that recommendations as to the best clinical practice could not be based on scientific evidence.[57] Luckily, we have come a long way, as the TVT is revolutionary also in its breadth, type, and duration of study. The TVT is minimally invasive, can be performed as an outpatient procedure with minimal anesthetic requirements, and has minimal convalescence. There is always a chance of a delayed complication, especially in patients with adverse characteristics for transvaginal mesh surgery.

Intraoperative cystourethroscopy and a thorough physical examination should be performed in all patients undergoing sling surgery. This should be performed in the operating room at the time of mesh insertion to assure that the mesh was placed properly and did not injure the urinary tract or vaginal wall. I share the AUA's opinion that "any restriction of the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI."

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[56] Clemons JL, et al., Impact of the 2011 FDA Transvaginal Mesh Safety Update on AUGS Members' Use of Synthetic Mesh and Biologic Grafts in Pelvic Reconstructive Surgery. Female Pelvic Med & Reconstr Surg 2013 Jul/Aug;19(4):191–198.

[57] Black NA, Downs SH. The effectiveness of surgery for stress incontinence in women: a systematic review. Br J Urol 1996 Oct;78(4):497-510.

C. Mesh Characteristics and Response to Claims that There Are Better Alternatives

Plaintiffs' experts have attempted to come up with a classification system suggesting that one needs pore sizes of over 1,000 microns in all directions for tissue incorporation. It must be noted that this position is not held by AUGS, AUA, SUFU, ICS, IUGA, SGS, or NICE, or any other major medical society in this field. This is because this belief is solely a theory with no clinical support.

First, it is widely accepted that a Type 1 macroporous mesh is the appropriate mesh for SUI repair. This was specifically stated by NICE and the clinical data in women show that the TVT device has the optimal mesh characteristics. The Amid mesh classification published in 1997 defined the classification system as a Type 1 macroporus mesh.[58] A polypropylene mesh that is over 75 microns is a Type 1 macroporous mesh. Amid further did not assess simply infection, but also tissue integration to determine the appropriate pore size. Additionally, any notion that this classification was based upon the meshes available at the time and that a different classification should apply based upon the body's response to meshes again has no clinical support. The human body reacted to mesh the same way in the late 1990s as it does today.

In short, the TVT mesh is a Type 1 macropous mesh. Type 1 meshes have been the standard mesh used in SUI repair for the last 15 years. The pore sizes of the TVT are approximately 1,379 microns, one can see through the mesh in clinical application, and the pores are clearly large enough for tissue ingrowth, as the clinical data shows long-term efficacy.[59] I have seen this in my practice, the literature supports it, and if it were not the case, you would not see the substantial number of published articles showing that the TVT is the gold standard for SUI repair.

Furthermore, if a mesh implant does not incorporate, it may encapsulate and behave similar to a silicone or Gore-Tex implant. These implants are easily removed, as there is a capsule surrounding the material, as it never integrates into the native tissue. Encapsulation does not occur following TVT; rather, I note it to be consistently incorporated on revision cases that I have performed.

Based on short-term animal studies, some plaintiffs' experts have claimed that PVDF is a possible alternative to polypropylene. No professional associations have endorsed PVDF as an alternative to polypropylene. Further, there are no mid-term or long-term studies on PVDF used in the pelvic floor for the treatment of urinary incontinence. I am not aware of any hospitals in the United States using this material, and until there is clinical evidence to support its use, it would be irresponsible for physicians

[58] P.K. Amid, Classification of biomaterials and their related complications in abdominal wall hernia surgery, Hernia 1997;1:15-21.
[59] Pamela A. Moalli, et al., Tensile properties of five commonly used mid-urethral slings relative to the TVT, Int. Urogynecol J 2008;19:655–663.

to change to a completely different material. Others have also suggested the move to Ultrapro mesh for SUI. There are currently no manufacturers using a lighter-weight mesh with significantly larger pore for the treatment of SUI, and there is no short-term, medium-term, or long-term studies to support the use of Ultrapro mesh use over Prolene mesh for TVT. The single paper by Okulu cited by plaintiffs' experts does not even compare Ultrapro to TVT mesh. It does not look at any mid-urethral sling kit, and seems to be a modification of the earlier vaginal patch sling procedures that are no longer clinically relevant. The technique bears no resemblance to the TVT sling. The dissection involves a larger, inverted A incision, the mesh is transfixed to a vaginal island of tissue, passed using Prolene sutures that are then tied together over the rectus fascia. This is not a "tension-free" design. The mesh is hand-cut to varying sizes, and there is no sheath protecting the mesh. The sheath is a very important component to the TVT. Ultrapro is not compatable with a sheath, as it sticks and loses integretity during sheath removal. In this study, it is not directly stated that the mesh is even placed mid-urethrally. The extrusion rates are likely related to the type of incision and fixation of the mesh to the vaginal wall, neither of which are pertinent to TVT. It is my opinion that this study is irrelevant to the context of the TVT. Moreover, it pales in comparison to the volume and length of study of TVT. The urethra must have sufficient support, which is provided by the Prolene mesh. No other mesh with significantly different bio-material characteristics has been shown to have such good success rates and low complications for SUI treatment.

D. Infection After TVT

Ethicon further warns of the possibility of infections. Infections occur as often with native tissue repairs as they do with the TVT mesh. Further, because the TVT mesh has large pores and is made from polypropylene mesh, if an infection occurs, it can be treated most of the time without removal of the mesh, because the mesh does not potentiate infection and has pores large enough for the body to clean out the infection. Ethicon warns that in some cases of persistent infection, mesh removal may be necessary. Removal of foreign bodies because of SUI surgery is not isolated to TVT. It can occur when surgeons place non-absorbable sutures, as even sutures can become contaminated. Again, infection is not uncommon following incontinence surgery and is not necessarily a result of the mesh but of the patient's wound healing characteristics.

E. Inflammation After TVT and Claim of Cytotoxicity

Plaintiffs' experts have suggested that there may be an inappropriate inflammatory response with the TVT. This has not been the case in my practice, nor is there any literature from peer-reviewed urology, urogynecology, or gynecology journals that have demonstrated this to be the case. (See long-term studies referenced above, over 100 RCTs on the mesh do not demonstrate this. Professional statements do not support this.) In a study by Falconer, et al., the TVT was implanted and after two years a biopsy was

performed. It revealed that there was practically no tissue reaction to the TVT mesh.[60] This is consistent with what I have observed in my clinical practice.

Chronic inflammation and chronic inflammatory cells can be seen in vaginal tissue in the absence of mesh or another foreign body. The presence of chronic inflammatory cells does not mean that those cells are active. They can be quiescent. Plaintiffs' experts' claims that the mesh is continuously subjected to peroxides and other substances produced by chronic inflammatory cells are not accurate. If their contention was true, we would not see the superior cure, efficacy, and tolerability rates that have been shown in the literature and my personal experience. There would be essentially death of the tissues around this theoretical peroxide-exposed area with tissue necrosis in all TVT patients. The same can be said for claims that the mesh in TVT is cytotoxic in women. There is no reliable scientific data that shows that TVT is cytotoxic in women. To the contrary, the vast majority of patients have demonstrated efficacy with low complications. Mesh exposure occurs at a rate of approximately 1-3% in TVT patients as earlier noted in the Novara 2008 metaanalysis (1.1% vaginal erosion), Cochrane reviews such as Ogah 2011 (1.3% monofilament versus 6% multifilament) and Ford 2015 (2.1%), Tommaselli 2015 systematic review and meta-analysis of medium and long term complications (Fig. 6, 2.1%) and the 2014 SGS systematic review by Schimpf, et al. (1.4%). The long-term data do not show cytotoxicity, and their results are contrary to plaintiffs' experts' theories. If the mesh were cytotoxic, the tape would be rejected in all of the women and the tissue would die, becoming necrotic. This is not relected in the medical literature.

In the actions section in the IFU, Ethicon informs physicians that the mesh elicits a minimal inflammatory reaction in tissues that is transient. From a physician's standpoint, I am concerned about a persistent acute inflammatory response that has a clinical effect on patients. The Ethicon IFU tells me that there will be an acute inflammatory response to insure the tissue integrates into the mesh, but that this acute inflammatory response is transient. On a microscopic level, there will be a minimal-to-mild chronic inflammatory response, but as this has no clinical effect on patients, it is not a concern for me or any other reasonable physician. This section properly tells physicians about the clinical implications of the inflammatory response. It also tells physicians that the tissue will incorporate into the mesh; therefore, if removal is necessary, it is explicit that you will have to cut around the tissue to explant the mesh. This tells an incontinence surgeon exactly what would be necessary to remove the mesh and the implications for the patient.

F. Claims of Contracture After TVT

TVT mesh does not curl, contract, or experience pore collapse when placed in vivo in accordance with the IFU. The sheath protects against tissue trauma and helps the mesh slide through the tissue while keeping its shape. The mesh itself does not contract.

[60] Falconer C, Influence of Different Sling Materials on Connective Tissue Metabolism in Stress Urinary Incontinent Women. Int Urogynecol J 2001;(Suppl 2):S19-S23.

Scar tissue contracts in any pelvic surgery. The design of the mesh allows incorporation of tissue and reduces the risk of infection. Surgeons are aware, as with any implantation of a foreign body, there are acute and chronic inflammatory cells. The inflammation with TVT is minimal. Inflammation is a normal and necessary part of tissue in growth and wound healing.

Plaintiffs' experts have indicated that contracture may occur with transvaginal mesh, leading to side effects. If the TVT mesh had significant contracture, then you would expect to see uniformly the mesh contracting, chronically elevating the bladder and almost all patients with voiding dysfunction. The clinical literature again does not support these propositions. Clinically significant tissue contraction is a rare complication.

G. Claims of Degradation After TVT

Clinical evidence does not show that the TVT mesh degrades or that if it did it leads to a clinically significant effect. Long-term clinical studies show lasting success, low to no late-term complications, and are inconsistent with degradation theory. Studies like Clavé 2010[61] do not account for handling and alteration during processing prior to analysis. Clavé 2010 is unreliable and fails to show degradation. The sample analyzed in that study was less than 1/3 of the overall cohort (32 out of 100) and no selection criteria was described. The authors also failed to discuss whether any damage to the mesh occurred during surgical explantation. The SEMs showing surface cracking could be from biologic material and handling, as well as preservation. Moreover, the chemical analyses performed do not show degradation. Likewise, the Costello study[62] sometimes relied upon by plaintiffs' experts was a case report, which is unreliable and concerned a Bard mesh. One must also remember that biologic materials in slings, as well as autologous and cadaveric fascia are known to degrade.[63]

Plaintiffs' experts indicate degradation may take place with the TVT. From a clinical standpoint, I have never seen the TVT mesh degrade or cause any clinical effect. I have not witnessed any gross evidence of mesh degradation on surgical revision cases. If somehow the mesh did microscopically degrade, there has been no clinical effect. Moreover, I have never read or seen a single peer-reviewed published article (or seen any cited by plaintiffs' experts) that showed any clinical effect of degradation.

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[61] Clavé A, et al., Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants. Int Urogynecol J 2010;21:261–270.

[62] Costello CR, et al., Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants From a Single Patient. Surgical Innovation 2007;14(3):168–176.

[63] Woodruff A, et al., Histologic Comparison of Pubovaginal Sling Graft Materials: A Comparative Study. Urology 2008;72:85–89.

H. Claims of Cancer After TVT

There is no reliable scientific information to support the claim that polypropylene can cause cancer or sarcoma. I have not personally witnessed cancer from mesh in any patient that I have implanted with PP in 15 years, and after more than 1,000 surgical implants. My experience is consistent with the clinical literature.[64] Moreover, the scientific data does not support plaintiffs' experts' contention that the TVT presents a risk of sarcomas or cancer. There are no reports in the medical literature of tumors related to the implantation of surgical-grade polypropylene for midurethral slings, and there is no evidence suggesting any carcinogenicity in humans related to polypropylene despite hundreds of millions of individuals being implanted with the material in various forms for well-over a half century.[65] The Prolene material that the TVT mesh is comprised of has been used for decades, and studies do not show a statistically significant risk. There was no need for Ethicon to warn of this alleged risk in the TVT IFU.[66]

The rate of late complications and erosion with TVT device is very low, and the long-term data demonstrates that the TVT mesh has long-term biocompatibility. Thus, plaintiffs' experts' contentions and theories regarding the weight and pore size of the mesh, the way it is cut, its purported tendency to degrade, cause inflammation, and be cytotoxic are not scientifically reliable and contrary to the clinical data.[67]

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[64] King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453

[65] AUGS & SUFU, Frequently Asked Questions by Providers—Mid-urethral Slings for Stress Urinary Incontinence. (available at http://www.augs.org/p/bl/et/blogaid=194); Dwyer PL and Riss P, Carcinogenicity of implanted synthetic grafts and devices. Int Urogynecol J 2014 May;25(5):567–568.

[66] Moalli P, et al., Polypropylene mesh: evidence for lack of carcinogenicity. Int Urogynecol J 2014, DOI 10.1007/s00192-014-2343-8; King A, et al, Current Controversies Regarding Oncologic Risk Associated with Polypropylene Midurethral Slings. Curr Urol Rep 2014;15:453; Sunoco MSDS; AUGS & SUFU, Frequently Asked Questions by Providers—Mid-urethral Slings for Stress Urinary Incontinence. (available at http://www.augs.org/p/bl/et/blogaid=194).

[67] Laurikainen E, et al., Five-year results of a randomized trial comparing retropubic and transobturator midurethral slings for stress incontinence. Eur Urol 2014 Jun;65(6):1109-14; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J 2013 Aug;24(8):1271-8; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol 2012 Nov;19(11):1003-9; Aigmueller T, et al., Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol. 2011 Nov;205(5):496.e1-5; Serati M, Tension-free Vaginal Tape for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 10-Year Follow-Up, European Urology 2012;61:939-946; Olsson I, et al., Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence, Int Urogynecol J 2010;21:679-683; Liapis A, Long-term efficacy of tension-free vaginal tape in the management of stress urinary incontinence in women: efficacy at 5 and 7 year follow-up, Int. Urogynecol J 2008;19:1509-1512.

V. INSTRUCTIONS FOR USE

A. Overview

In my medical training, I have been trained on risks associated with incontinence repairs. In addition to this training, I have performed hundreds of incontinence repairs and keep apprised of the current literature; therefore, I know the risks associated with the TVT and other incontinence repairs. The risks with TVT are common to other incontinence SUI procedures with the exception of mesh erosion. Based upon my training, education, experience, and review of literature, the instructions for use (IFU) for the TVT device adequately warns surgeons of the risks associated with the TVT. The most common risk of all SUI surgeries is urethral obstruction leading to urinary retention. This is also the most common risk with TVT, and can occur regardless of graft material.

As a urologist, I review IFUs for devices that may be used in the pelvic floor and other areas in my practice. I have reviewed many IFUs for different devices used in my medical practice. From a physician's perspective, it is my opinion that the IFU for TVT appropriately sets out the indications, warnings, and precautions, adverse reactions, and contraindications associated with the use of the device.

It is important that the IFU indicate both the ideal patient for the TVT procedure as well as the type of surgeon who could perform this procedure. After the paragraph that says "Please read all information carefully," there is a section identified as being "Important." In this paragraph, Ethicon informs physicians "this device should be used only by physicians trained in the surgical treatment of Stress Urinary Incontinence and specifically implanting the Gynecare TVT device." Under the "Warnings and Precautions" section, the third bullet again warns, "Users should be familiar with surgical technique for bladder neck suspensions and should be adequately trained in implanting the Gynecare TVT System before employing the Gynecare TVT Device." As a physician, this signifies that this device is intended, not just for just any surgeon, but only those surgeons who have experience with SUI repairs. The IFU specifically tells physicians that they should be trained on the device. This additional training may come from Ethicon or from other surgeons experienced with the TVT or similar midurethral slings.

From a surgeon's perspective, the warnings in the IFU are appropriate and include all necessary warnings. I will specifically note a few of them. Ethicon informs physicians to manage infections with regard to their normal practice. The TVT mesh is made with a material that does not promote infection, and it will allow the body the opportunity to resolve mesh infection without removal in most cases. However, Ethicon does warn that should persistent mesh infection occur, mesh removal could be necessary in a small number of cases.

As with other incontinence procedures, Ethicon warns that de novo detrusor instability may occur following the TVT procedure, but to minimize this risk, the surgeon

should ensure the tape is tension-free. With any surgical procedure for incontinence, detrusor instability can occur. It will occur more often with the Burch or MMK than with midurethral slings because of the chronic tension on the urethra inherent in the Burch and MMK procedures. The TVT is superior to most incontinence procedures with respect to reducing the risk of detrusor instability due to urethral obstruction due to the tension-free nature of the device.

The TVT IFU specifically discusses the adverse reactions associated with the TVT. In my opinion, the IFU appropriately identifies the adverse events associated with the TVT. The adverse reactions section identified those potential adverse events that are directly associated with the product. It is my opinion that Ethicon has properly warned physicians of the adverse events that can result from a TVT procedure.

Ethicon enumerates adverse reactions, including laceration of vessels, nerves, bladder, or bowel may occur during needle passage, and may require surgical repair. Ethicon has previously warned physicians that the TVT procedure should be performed with care to avoid large vessels, nerves, bladder, and bowel. Attention to local anatomy and proper passage of needles will minimize risks. With any procedure in the pelvic floor, there is the risk of nerve injury, and with many procedures the risk of bladder and bowel injury. Ethicon informs physicians that they must understand the pelvic anatomy to avoid such injuries. Ethicon informs the surgeon that is imperative to follow the IFU when performing the TVT procedure to avoid such injuries in most cases.

Ethicon warns that erosion, extrusion, and fistula may occur following TVT. Mesh exposure is uncommon with midurethral slings such as TVT, and occurs in only 1-2% of patients. Usually, exposure can be successfully managed with estrogen cream or by trimming of the exposed portion of the sling. For some small asymptomatic mesh exposures, observation is even an option. Pelvic pain from an exposed mesh will usually resolve following trimming or partial excision.

Intra-operative bladder perforation from the trocar has been shown to occur in approximately 4-7% of patients with the TVT; however, the clinical significance of a recognized bladder perforation is minimal. It is imperative that the physicians perform a careful cystoscopy. Cystoscopy is a crucial step when performing the TVT procedure and there is an additional warning that cystoscopy should be performed. Cystoscopy will recognize bladder perforation, and allows for the repositioning of the trocar and mesh into the proper position. This is specifically identified as a proper procedural step and identified in the warnings as bladder perforations can occur, but when performing cystoscopy they can be properly identified and then corrected intra-operatively with no clinical harm to the patient.

Chronic urinary tract perforations or fistulae from TVT are uncommon. They do require more advanced reconstruction in many instances, and are almost always the result of mesh that was placed with an undue amount of tension and a delay in TVT lysis. Mesh

erosion (perforation) into the bladder is usually due to an unrecognized bladder perforation at the time of mesh implant or mesh that was inadvertently tunneled in the wall of the urinary tract. These complications can be resolved either using an endoscopic, laparoscopic, or open approach.

Bowel and major vessel injuries can be more significant, but very rarely occur. Bowel perforations may occur more commonly in patients with a history of peritonitis, bowel surgery, ruptured appendix, or known extensive pelvic adhesions. Hematomas that occur from a lacerated vessel are rare (1-2%) and usually not life-threatening. Major vascular injury occurs in less than 0.5% of patients. It should be noted that laceration of vessels, nerves, bladder, or bowel might occur with any urinary incontinence procedure.

Nerve pain is usually a result of nerve entrapment or irritation, but can occur if a nerve is lacerated. These can occur if the mesh is placed too close to a nerve. This usually results from misplacement of the mesh in too lateral of a location. Most nerve pain is treated with medication, trigger point injection, and physical therapy, and does not require surgical intervention. Chronic pelvic pain from nerve injury occurs more commonly as result of traditional SUI procedures. When you chronically elevate the urethra and attach sutures to a bone anchor, there is an increased risk of pain from tension and bone irritation.

Plaintiffs' experts' reports and/or depositions indicate that pain and dyspareunia are not addressed in the IFU. I disagree with this opinion, as a reasonable surgeon would understand that pain and dyspareunia are potential symptoms of many of the adverse events that are listed in the IFU, including puncture or lacerations of vessel, nerves, bowel or bladder, fistula, inflammation, erosion, infection, and over-tensioning of the mesh. Any of these adverse events may cause pain. Pain and dyspareunia are commonly known by both experienced and new surgeons to occur following incontinence procedures. Similarly, Ethicon does not warn physicians of bleeding, because any surgeon knows that lacerating a vessel can cause bleeding. The IFU also does not assert that the nerve puncture or laceration, fistula, or other adverse events are only temporary, but says they can occur, which means they can be short-term or long-term. It is commonly known by physicians that when you implant a permanent medical device that the complications can occur in the short or long term. It is my opinion that most adverse events listed in the IFU resolve, although long-term complications may occur in rare and uncommon situations.

There was no need for Ethicon to warn of this alleged risk of cancer in the TVT IFU, as this is not supported by the medical literature.

The TVT IFU is adequate. Professional education supplements the IFU. Both teach of risks and avoidance of complications as well as specific steps of performance. Professional education included discussion of complication management. Furthermore, the Patient Brochure for the TVT device is a resource for additional information. But it is

not meant to supplant the informed consent process. It includes information on complications. I have conducted numerous professional education activities including proctorships, cadaver labs, and lectures where I taught based on the IFU and provided information regarding device usage, potential complications, and the management of those complications to hundreds of surgeons around the country. This would include TVT, TVT-O, and TVT Abbrevo.

In summary, serious complications are uncommon and major intraoperative complications are rare. The IFU, patient brochure, professional education, medical literature, and the FDA Public Health Notification of 2008 discuss potential complications, including exposure and pain/dyspareunia. There is no medical device that is without any potential complications, and SUI devices like the TVT are not exceptions to this rule. With that said, there is no alternative procedure for SUI that has a superior risk-to-benefit ratio compared to the TVT device. For that reason, the TVT device remains the procedure of choice and the gold standard for physicians and patients with SUI.

B. TVT Tensioning Discussion in IFU

The IFU states that the TVT is intended for the treatment of SUI for female urinary incontinence resulting from urethral hypermobility and/or intrinsic sphincter deficiency. The TVT is an appropriate device for both of these indications, and is able to correct the mechanisms of each, as described above.

Ethicon warns that putting too much tension on the tape may cause temporary or permanent lower urinary tract obstruction. This is simply saying that too much tension can cause temporary or permanent urinary voiding dysfunction. Cystitis and temporary voiding difficulties are the most common problems after an incontinence procedure. This temporary voiding issue is at least partially related to the surgery itself and the duration of postoperative catheterization. In most cases, normal voiding resumes within a few days. This is why it is important to follow the IFU and ensure there is a drop or two of urine when the TVT is placed. This helps to ensure that voiding dysfunction is limited. Voiding dysfunction is a much larger issue with the Burch and MMK because the urethra is chronically elevated. Long-term voiding dysfunction is rare with TVT, but if it does occur, it is because the TVT was not placed in the right location on most occasions. If it needs to be treated, then one can likely cut the mesh to relieve the tension. On extremely rare occasions, mesh removal is indicated.

The IFU describes how to maintain the appropriate tension on the tape for support for the urethra to prevent SUI. The surgeon is informed to fill the bladder to approximately 300 ml and use patient feedback to determine tension, i.e. a cough test. Ethicon specifically describes how to also ensure the tape is placed tension-free. This means the tape is not chronically elevating the urethra as is done with the Burch colposuspension. To avoid putting tension on the tape, a blunt instrument (scissors or

forceps) should be placed between the urethra and the tape during removal of the plastic sheaths.

VI. TVT PATIENT BROCHURES

The purpose of the patient brochure is to facilitate a conversation between the patient and her physician. The brochure properly identifies the disease state, options for women, and the potential complications. The brochure makes it clear that this surgery should be performed only after a complete physical examination.

The patient brochure serves to merely introduce the TVT device. It is not a substitute for a consultation with the surgeon. It is the surgeon's job to inform the patient of the risks and benefits of the procedure. It is the surgeon's responsibility to answer the patient's questions and decide if the patient is an appropriate candidate for TVT after discussing the risks, benefits and alternatives. A brochure is never a substitute for this discussion.

From my review of the brochures for TVT, TVT-Obturator, TVT-Secur and TVT-Abbrevo, I can see that options including non-surgical treatments are discussed. Ethicon provides detail on risks and benefits for the procedure. Again, it is emphasized in the brochure that you should consult with your physician to discuss the risks and benefits, and only after this discussion should the device be implanted. The brochure provides an overview of the procedure in layman's terms, but never is a subsitute for informed consent.

VII. PROFESSIONAL EDUCATION

A. Introduction

I became familiar with the Ethicon Professional Education Program when I attended a course on the TVT-Obturator in San Francisco on March 23, 2004. This was a lecture session. The course faculty reviewed the proper patient selection, indications for the procedure, and surgical dissection. Afterwards, there was a laboratory session at a nearby facility where physicians were instructed on how to use the device on a cadaver. This was a hands-on laboratory session, where experts on the procedure who were preceptors for Ethicon instructed physicians. The preceptors guided the new users on how to properly perform the procedure.

In December of 2004, I became a preceptor for Ethicon on the TVT procedure. I functioned as a preceptor for Ethicon from 2004-2011. I have personally instructed physicians on how to perform the TVT, TVT-Obturator, TVT-Abbrevo and TVT-Secur on numerous occasions in small group settings referred to as preceptorships or proctorships by Ethicon Professional Education Department. I have also been one of three-to-five faculty members at Ethicon-sponsored didactic/cadaver courses where

typically 10-20 physicians would attend and be instructed by a small group of faculty members.

B. Phases of Program

The Ethicon professional education program involves a didactic portion where physicians attend a course with the designated topic such as incontinence, prolapse, or both. This includes 3-4 hours of didactics overviewing patient selection, surgical technique, and long-term data on the device. Surgeons may then attend a cadaver lab, direct observation in the operating room where surgeons will be invited into the OR and observe an experienced surgeon perform the TVT procedure (preceptorship), or attend a proctorship where the proctor for Ethicon would be a guest in another surgeon's operating room and directly observe a TVT procedure to serve as a reference on how to properly use the surgical kit provided by Ethicon.

In my experience as an attendee, preceptor, and proctor, I never observed or experienced "pressure" by Ethicon to convince attendees that their products should be placed without preexisting knowledge of pelvic anatomy or without regard to individual patient characteristics. I observed that the courses simply taught physicians how to use the kit properly. The preceptorships allow new users to witness experts placing the device. Proctorships provide an opportunity for new users to have their initial cases overseen by an expert.

C. Complication Prevention and Management

There was a continuous and collaborative effort to identify and implement ways to avoid complications. There was review of how and why complications occur. At bi-annual meetings and summits, the education panel would receive information on complications and then provide feedback to TVT users on how to prevent these complications. The group also made presentations on complications and algorithms to manage adverse events. This allowed for improvement in surgical techniques and helped better identify who was an appropriate candidate for the procedure. There was significant education provided on how to recognize and treat mesh-related complications such as exposure, erosion, and pain.

Preceptors, as well as Ethicon professional education staff, were available to their trainees to discuss complications and provide advice on how to effectively manage complications. This close network allowed rapid bi-directional feedback from the company to the physicians.

D. Credentialing

The Ethicon Profession Education Program is not a credentialing process. Although Ethicon provided attendance certificates, this certificate did not purport to "certify" the physician as being proficient at performing the procedure.

The certificate from the program simply documents the surgeon's attendance at an Ethicon Professional Education Event. It shows that the physician made an attempt to be educated on the procedure. The actual credentialing for performing any surgical procedure should always occur at the hospital level, and it is up to the physicians on an appropriate hospital committee to decide which procedures the surgeon is capable of performing.

Furthermore, it is the physician's responsibility to know the pelvic anatomy, to understand biomaterials, and to properly select patients for the procedure. TVT is merely a kit to help the surgeon place a mesh graft in the vagina using a trocar system for anchoring. Tunneling the trocar decreases the amount of dissection required and allows a reliable anchoring mechanism for the graft. The TVT system does not in any way make the surgeon competent in anatomy, proper dissection, tunneling, graft deployment, or wound closure. Credentialing is done at the level of the hospital by a review board. It is not the responsibility of Ethicon to credential surgeons on TVT.

VIII. PRODUCT DESIGN

Design of the mesh and TVT are suitable for use in SUI mesh repair. The mesh used in TVT is state of the art and considered the gold standard for first line treatment of SUI. It has the most RCT data and long-term data supporting safety and efficacy to 17 years. Efficacy in these studies is generally consistently in the 80-90% range, with low complications and very few late-term complications.[68]

TVT is an important SUI device that has ideal design features. It is an extremely useful device to treat stress urinary incontinence. It is a Type 1 large-pore-size polypropylene mesh, and is the most commonly used mesh in the history of incontinence surgery. The design of the mesh, the surrounding plastic sheath, the trocar, and the tension-free system has offered a minimally invasive approach to stress urinary incontinence surgery, which is of benefit to patients and surgeons. The large pore size of the mesh reduces the risk of infection. The Prolene mesh is the most widely used in the world. The mesh allows tissue incorporation while suspending the urethra and providing a backboard of support, which is consistent with the Ulmsten theory of stress urinary incontinence surgery. And because the mesh is made of a synthetic material, it avoids cultural or religious objections that some patients have to the use of xenografts or

[68] Nilsson CG, Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. Int Urogynecol J 2008;19:1043-1047.

allografts. This attribute also leads to high efficiency and longevity while xenografts and allografts can be resorbed by the body. The device's utility is also seen in the fact that it is comprised of a material that has been in use in various applications for several decades and the body's reaction to it is well-known.

Additionally, the sheath on the mesh is useful in that it carries the load of implanting the mesh, allows the placement to be optimized, and reduces the risk of infection. Once it serves those functions, it can then be removed once the mesh is properly placed.

Since stress urinary incontinence is such a prevalent condition, a device was needed to treat this problem safely, efficiently, and effectively. Previously, incontinence surgeries were performed by only a select number of surgeons. The TVT device has been shown to be safe and effective in not only expert hands, but also in the hands of general urologists and gynecologists in a community setting. Considering the prevalence of stress urinary incontinence, it would be impossible for a few experts around the country to meet the needs of society. As the TVT device standardized stress urinary incontinence surgery and allowed tensioning of the mesh in a straightforward manner, this allowed for greater applicability of the device, making it extremely useful in the community. The TVT device allowed patients to be treated locally, and no longer did they need to travel long distances to a university or a tertiary setting in order to have the gold standard procedure for stress urinary incontinence.

The utility of the TVT device is also seen in that it can be implanted in an outpatient procedure in as little as 20-30 minutes using very small incisions. Most patients can drive a car the next day and resume working within two days. They can return to normal exercise in just one week. The open procedures are more morbid and require longer convalescence. Such factors are important considerations with respect to the direct costs of longer operative times and postoperative hospitalization, as well as the indirect costs related to loss of work due to a comparatively longer convalescence.

TVT is a safe product that is no more likely to cause injury to surrounding structures such as the bladder, the ureter, the intestine, or nerves than traditional native tissue repairs for incontinence such as the pubovaginal sling or Burch procedure. All SUI surgeries—including native tissue repairs—can have side effects such as bleeding, infection, pain, and dyspareunia. None of these complications are unique to transvaginal mesh used in the TVT system. The mesh-related complications that occur with TVT can occur with biological tissues such as allograft and xenograft. Additionally, permanent features such as Ethibond, Prolene, and Gore-Tex have been shown to have a risk to become exposed overtime. Again, this is not a unique complication to polypropylene mesh.

The TVT kit was designed with a narrow trocar that can be tunneled through the retropubic space and has a surrounding plastic sheath. These features allow safe

placement of the polypropylene mesh. Plaintiffs' experts may argue that this procedure is done blindly. But the TVT procedure is no more blind than a needle carrier being passed across the retropubic space during a traditional sling procedure. It is no more blind than a trocar placed in the abdomen during laparoscopic surgery. It is no more blind than a Foley catheter being placed in the urethra or an intravenous catheter. It is common in medicine for a physician to pass a medical device through tissue when the surgeon is familiar with the anatomy. The advantage of this passage is that it minimizes the dissection, which minimizes time, bleeding, postoperative pain, and the significant risks and morbidity that arise with an open procedure. Moreover, cystoscopy is recommended, and when there is a bladder perforation noted, it is not a significant complication, as the trocar can be repassed and the bladder will heal on its own.

Additionally, the TVT has a unique way of allowing a tension-free support to the urethra. The tension-free concept had never existed in surgery before the TVT device. The most common complication with the traditional SUI procedures is urethral obstruction leading to incomplete bladder emptying and urinary retention. This occurred in as many as 10 to 20% of patients and led to re-operation to loosen the suspension sutures or to cut the sling.

Finally, autografts need to be harvested from the patient's abdomen or leg and may lead to harvest site complications such as abdominal wall hernia, wound complications, infection, nerve injury, and leg pain. Finally, the severity of TVT complications is usually minor. In fact, if there is an exposure, many are managed medically. Where needed, such as in the case of a larger exposure, most can be treated with minor excision of exposed mesh. If the complication is managed properly, it should not result in multiple operations.

Pelvic surgeons, investigators, and industry have been interested in graft material for stress urinary incontinence for many years in efforts to improve the outcomes in SUI surgery. This process has evolved over 20 years. TVT has the ideal balance of large pore size to allow tissue ingrowth and local tissue tolerance. It has been cleared by the FDA since 1998, and is the most common SUI procedure performed to date. In order to best understand the value of the TVT device, we need to recall the history of SUI surgery. There have been many synthetic materials that have been used in SUI surgery dating back to the 1960s, with Muir reporting on use of Mersilene and Morgan reporting on the use of Marlex.[69] However, these and other meshes were not tolerated to the extent that TVT was, which is why all of the pertinent professional societies, SUI guidelines, and Cochrane reviews recognize the type 1 TVT macroporous mesh as being the best-suited for SUI. Plaintiffs' experts contend that TVT mesh is a heavyweight mesh. However, the literature, my personal experience, and those of other experts clearly show that TVT is

[69] Moir JC. The gauze-hammock operation. (A modified Aldridge sling procedure). J Obstet Gynaecol Br Commonw. 1968 Jan;75(1):1-9; Morgan JE. A sling operation, using Marlex polypropylene mesh, for treatment of recurrent stress incontinence. Am J Obstet Gynecol. 1970 Feb 1;106(3):369-77.

not a heavyweight mesh, nor does it behave like one. It is specifically recognized that the TVT mesh in the SUI application is "macroporous, monofilament, light weight polypropylene" and it has demonstrated long term durability, safety, and efficacy in several studies as I earlier referenced, up to 17 years.[70]

Allografts and xenografts may be considered for SUI surgery. However, allografts can weaken with time leading to delayed failures. Additionally, these materials are rejectionable due to cultural and religious beliefs. For example, patients who are Jehovah's Witnesses or Native Americans refuse to allow tissue transfer from the deceased. Xenografts offer an alternative to allografts as they avoid disease transmission and the cultural concerns of cadaveric tissue. However, they have been shown to cause an intense immune reaction that can lead to extrusion and healing abnormalities. Bovine products have largely replaced porcine products and are interesting, but the data currently does not exist in SUI surgery. Rather, bovine products have only been studied in prolapse cases. The TVT mesh does not transmit disease, nor does it cause an immune reaction, and it is less expensive than allografts or xenografts, and remains the gold standard material for SUI surgery. The general public, pelvic surgeons, and others are very familiar and widely accept polypropylene mesh for the use in hernia surgery. Similarly, it is not surprising that women are readily accepting of transvaginal polypropylene mesh for SUI surgery.

Alternatives to mesh and alternative trocar designs:

- Other Trocars or Instruments—TVT Exact trocars are functional, but not overall safer.

The TVT Exact trocar is slightly smaller than the classic TVT trocar, but performs in a similar manner. There is no data to suggest the smaller trocar is safer.

- Transobturator Slings—these are good to have in the surgeon's armamentarium, but there is not as much data on them compared to the TVT retropubic sling, and they carry a higher risk of temporary groin pain compared to retropubic slings.

The advantage of the TVT-O kit is that it allows mesh to be placed with avoidance of the retropubic space. The TVT-O procedure has a decreased risk of urinary retention due to urethral obstruction and bladder injury when compared to TVT. However, TVT-O has been shown to cause more short-term groin pain, and is not as effective in treating patients if they have a

[70] AUGS-SUFU Position Statement on Mesh Midurethral Slings for SUI, 2014 Jan.

low leak-point pressure.[71] Moerover, it is not as effective for patients with more severe incontinence due to intrinsic sphincter defeincy.[72]

While transobturator and mini slings are available to surgeons, the overall data do not show they are superior to the TVT. And like all SUI surgeries, they have potential complications including potentially more early groin pain for the transobturator route and potentially decreased efficacy in some surgeons' hands for mini slings, which has been reported. The overall data show that the rate of serious complications with the TVT such as ureteral or bowel injury is rare, and while there are higher rates of bladder perforation with the TVT, with cystoscopy performed as recommended by the IFU this complication is easily managed and does not lead to any long-term effect.

- No sheath—mesh would drag and stretch too much, placement adjustment would be more difficult, mesh would not be protected during passage.

If there was no plastic sheath covering the polypropylene mesh it would create greater friction when placing the mesh. Potentially, this can lead to displacement or improper tensioning on a full-length sling. Additionally, tensioning and minor adjustemtns after tunneling the mesh would be more difficult.

- Multi-filament mesh—increased immediate inflammatory reaction, increased risk of infection

Multifilament meshes (Amid Type 2 and 3) have been used in the past and have been shown to have more compications when compared to a Type 1 polypropylene mesh. Type 2 multi-filament meshes have small pore size and result in increased inflammation and carry an increased risk of infection. They do not incorporate into the surrounding tissue and can encapsulate and behave like a foreign body.[73] In vivo, the Gore-Tex sling (Type 2) becomes covered with a pseudocapsule, which significantly deters tissue integration and propagation of cell growth. Rates of rejection appear to be directly related to sling length because full-length slings have been

[71] Fong EDM and Nitti VW, Mid-urethral synthetic slings for female stress urinary incontinence. Br J Urol Int 2010;106:596–608; Latthe PM, et al., Two routes of transobturator tape procedures in stress urinary incontinence: a meta-analysis with direct and indirect comparison of randomized trials. Br. J Urol Int 2009;106:68–76.
[72] Miller JJ, et al., Is transobturator tape as effective as tension-free vaginal tape in patients with borderline maximum urethral closure pressure? Am J Obstet Gynecol 2006;195:1799–1804.
[73] Kobashi KC, et al., Erosion of woven polyester pubovaginal sling. J Urol 1999 Dec;162(6):2070–2072.

associated with excision rates exceeding 30%.[74] Therefore, multifilament mesh should not be used for SUI and POP surgery.

- Extra-large-pore mesh—no good data supporting this, would have more recurrences, not tested to 17 years, still would have risk of exposure

According to Amid, a macroporous mesh such as TVT has a pore size > 0.75 mm. Extra-large-pore size mesh such as those used in prolapse surgery in general have a pore size of 2.5 mm or greater. Unlike the TVT family of products, extra-large-pore mesh such as an Ultrapro does not have any short, intermediate, or long-term data to support its use for SUI. In theory, it may sound attractive, but it has not been tested in SUI surgery for 17 years like TVT. Additionally, pore size of 2.5 mm would not eliminate the risk of exposure, as most mesh exposures are related to wound healing abnormalities and technical failures.

- Laser-cut mesh—no difference in clinical and physiologic range, just an aesthetic difference, any particles from MCM do not cause harm—it's the same Prolene as one puts in in much greater volume for suspensions and other surgeries

There is no differemce between laser-cut mesh and mechanically cut mesh in the clinical or physiologic range; the stiffness of the mesh is the same for both products. Laser-cut mesh has less fraying of particles upon implantation but the effect of fraying is not clinically relevant based on my own personal observation and review of the literaure.

Any suggestion that the TVT device should undergo continuous modification is completely unrealistic, unnecessary, and ill-advised. If the TVT product was constantly altered in terms of pore size, length, or other design characteristics, it would be impossible to collect long-term data on these products. Instead, it was robustly studied, and continued to show efficacy and safety year after year. That is why it became the gold standard mesh in the SUI application, and as more and more data were published and presented, it became clear that the 1.1 cm strip of mesh was optimal for its intended use to support the midurethra and treat stress urinary incontinence. The TVT product has been performed in more than 3 million patients worldwide since 1998. The mesh was initially produced by mechanically cutting the product. In 2008, the mesh was laser cut. The literature clearly shows that there is no difference in the performance of the mesh regardless of how it was cut in the factory. My own personal experience with the device

[74] Weinberger MW and Ostergard DR, Postoperative catheterization, urinary retention, and permanent voiding dysfunction after polytetrafluoroethylene suburethral sling placement. Obstet Gynecol 1996 Jan;87(1):50–54.

both before 2008 and after 2008 is consistent with this statement in that I have not noticed any appreciable outcome difference in terms of complications, fraying, stiffness, tolerability, tensioning, or efficacy.

The pelvic surgeon's ability to avoid danger by exercising care and the use of the TVT product is dependent on the surgeon's medical school education, residency training, and clinical experience. In order to avoid danger, the pelvic surgeon needs to have familiarity with the anatomy in order to avoid complications to surrounding structures. This knowledge is necessary when performing any type of stress urinary incontinence procedure, and is not a knowledge base that needs to be developed or is unique to the TVT product. It is expected of pelvic surgeons to know the anatomy in which they choose to operate. Rather, once the surgeon has a fundamental knowledge of the anatomy, then the TVT device can be used safely. In order to exercise care in using the device, the surgeon should be familiar with the IFU included in the surgical packaging. Also, the surgeon should be intimately familiar with the medical literature, the information provided by professional education, and should network with pelvic floor surgeon colleagues. There are a number of important professional education events including cadaveric labs, surgical videos and animations, PowerPoint presentations, and most importantly, closed discussion with colleagues, mentors, and partners that allow the surgeon to exercise caution when placing the TVT device.

The surgeon's anticipated awareness of the dangers inherent to the TVT product and the surgeon's ability to avoid danger is part of the general knowledge of pelvic floor surgeons or contained in the device's IFU. Surgeons that have experience with traditional native tissue repairs should be aware of the pelvic anatomy and the steps necessary to perform SUI surgery safely. These surgeons would and should be aware of the complications with potential SUI surgery that are taught in their medical school, residency, and fellowship, and are obvious based on their base knowledge as surgeons, as well as their clinical experience performing colposuspension and sling procedures. These are basic / elemental surgical risks:

a. Damage to bladder, bowel, ureter, nerves and vessels

b. Infection

c. Inflammation and scarring

d. Wound complications like exposure, erosion, wound dehiscence, wound herniation, hematoma, seroma, pelvic abscess

e. Pain, pelvic pain/groin pain and dyspareunia

f. Bowel or bladder dysfunction

g. Fistula

h. Anesthetic risks

i. Need for reoperation and/or further treatment like catheterization or surgical revision

j. Failure of the operation requiring reoperation

k. PE, DVT, MI, pneumonia and death

l. Bleeding

Further, complications are known to occur and range from not troubling, mild, moderate or severe, temporary or chronic. This is basic surgical knowledge that all pelvic floor surgeons would know or would be expected to know. Risks of stress incontinence surgery are also a topic of testing in the various board certifications and the FPMRS subspecialty board. Moreover, experience with polypropylene mesh and with trocars has become commonplace in the last 20 years, as these procedures are now commonly taught in residency and fellowship training programs. It has become a core procedure and something that graduates should have a basic foundation in and understanding of both from their familiarity with pelvic anatomy from medical school and from their instructors during residency and fellowship.

I have read the IFU and have used it to help instruct residents, fellows, and physicians in practice on the proper use of the TVT. The IFU is a useful tool for surgeons in their practice, as it provides more specific detail about the TVT product, and is adequate. There is a separate IFU for each one of the TVT devices. Each device has its own unique safety profile, warnings for surgeons, and information on proper patient selection. However, the IFU should never substitute for surgical knowledge when selecting an appropriate patient and performing the procedure properly. This again is more reflective of the surgeon's skill set, training, and fund of knowledge. The IFU is merely a small portion of information that becomes part of the overall level of awareness of the dangers of the surgical procedure being performed. The most important component of the surgeon's awareness is their overall familiarity with pelvic anatomy and incontinence surgery.

There is a section on indications specifically for the treatment of SUI in women resulting from urethral hypermobility and intrinsic sphincter deficiency. The IFU outlines the key procedural steps including how to tension the mesh. There is a section on "Contraindications" within the "Warnings and Precautions" section. This section provides some guidance on proper patient selection, but does not substitute for the surgeon's experience or judgment. The IFU provides a list of adverse reactions. It discusses the possible puncture or laceration of vessels, nerves, bowel, or bladder, inflammation, erosion, infection and over-tensioning. It is common surgical knowledge

that any injury to these structures can result in pain. Ethicon warns in the IFU that these adverse reactions can be both short- as well as long-term complications.

IX. SUMMARY OF OPINIONS

A. Summary of my opinions is as follows:

- SUI is a widespread disease that affects many women. It has significant impact on patients' quality of life physically, emotionally, and socially. Surgical options are required for more severe forms of SUI.

- Traditional surgical options such as MMK and Burch are no longer the gold standard procedure for SUI today because they require abdominal incision, are time-consuming, have prolonged convalescence, have significant morbidity, higher rates of voiding difficulty, high rates of de novo pelvic organ prolapse, pain, and deteriorating results over the long term. Level 1 scientific data such as the Cochrane reviews, meta-analyses, the AUA SUI guidelines and the SGS systematic review all show that the TVT is effective, safe, and preferable to Burch and autologous slings. These data show that wound complications and sling exposures occur with these procedures and the rates of voiding dysfunction, pain, sexual dysfunction, and dyspareunia are lower with TVT than with the Burch and autologous slings.

- In most studies, fascial autologous slings generally do not show a success rate as high as TVT, and they have increased morbidity, operative time, pain, hospital stays, and convalescence when compared to TVT. The fascial sling is reserved for salvage situations and those with concomitant urethral pathology. Unlike TVT, fascial slings are only performed by a very small number of surgeons—mostly urologists—which would be incapable of treating the millions of women with SUI.

- Native tissue SUI procedures have been replaced in most community practices by retropubic or transobturator midurethral synthetic slings, which includes the TVT, TVT-O, and TVT Abbrevo. TVT, TVT-O, and TVT Abbrevo are synthetic mid-urethral slings which are used by more than 95% of pelvic floor surgeons.

- TVT is a truly revolutionary surgical procedure that changed the way SUI was treated. Dr. Ulmsten invented a procedure that allowed for mesh to be placed tension-free under the mid-urethra. This device has become the gold standard and the worldwide standard of care for treatment of this condition.

- The TVT is the procedure of choice for pelvic surgeons including urologists, urogynecologists, and gynecologists worldwide due to its reproducibility, safety, and efficacy.

- The TVT SUI products are the gold standard and standard of care for the surgical treatment of SUI and have been since 1998. The TVT is indicated for primary as well as many secondary cases of SUI due to urethral hypermobility and intrinsic deficiency. TVT is commonly performed in women following failed colposuspensions and fascial slings. There is good long-term efficacy and safety. The mesh used in the TVT is the most studied of any of the meshes used in stress incontinence surgery. It has been reported that there have been more than 3 million mesh slings sold since the mid-1990s. The TVT midurethral slings have been studied more than any other incontinence surgery. They have been assessed in both Ethicon-funded and independent studies.

- The TVT has significant benefits for the patient. Seventeen years of data, over 80 RCTs, and approximately 1,000 studies have shown that the TVT is safe and effective. The advantages over other procedures are that it has shorter operative time, reduced surgical pain, decreased hospitalization, reduced voiding dysfunction, quick recovery, extremely high success rates, and low complication rates. Further, long-term severe complications are extremely rare.

- All major professional organizations have declared that the TVT, both retropubic and transobturator, and similar midurethral slings are the standard of care for the repair of SUI. The AUA states that the data uniformly and overwhelming supports the use of midurethral slings (TVT) for the treatment of SUI, and as a result, it is the most commonly used procedure. I am a member of the AUA, and fully agree with this position statement as it reflects my personal experience.

- TVT is the standard of care for SUI. Along with similar midurethral slings, TVT is the recognized procedure of choice for SUI. Without this device and others like it, women's quality of health would be significantly diminished.

- TVT is not a heavyweight mesh, nor does it have small pore size. TVT is a Type 1 mesh and has pore size larger than and weight similar to other popular MUS such as Boston Scientific Advantage Fit and AMS Monarc. The AUA, AUGS, SUFU, and NICE all recognize that TVT is a macroporous, light-weight mesh (Amid Type 1).

- The TVT has an appropriate inflammatory response, integrates well in the body, provides the necessary support to the urethra, and adapts well. It is

not cytotoxic in women. Other meshes that have good quality evidence to support their uses have similar pore sizes, weight, and compliance for the intended use of treating stress urinary incontinence. Non-Type 1 meshes have been shown to be inferior to TVT macroporous mesh in the SUI application.

- Plaintiffs' experts reliance on animal, hernia, and prolapse documents and literature do not reflect the use of the 1.1cm strip of tape with the sheath in the configuration of the TVT placed under the midurethra in women, which is the TVT's intended use. These data are not reliable in the context of the TVT's use to treat SUI.

- TVT mesh does not degrade. The reliable scientific literature fails to show that the TVT degrades or that even if the surface cracking was degradation, that there is a clinically significant effect.

- TVT mesh does not cause cancer or sarcomas. The reliable scientific literature fails to show that the TVT mesh causes cancer or sarcomas.

- There is no clinical difference between mechanically-cut and laser-cut mesh employed in the TVT device.

- Pelvic surgeons who may use a TVT are expected to know the anatomy and potential risks due to their knowledge of fundamental and elemental risks with SUI and vaginal surgery. Risks with the TVT such as potential injury to organs, exposure of the mesh, voiding dysfunction, pain, and the need to potentially operate to treat complications are obvious based on a surgeon's fundamental knowledge and use of surgical instruments, the anatomy, wound healing, wound complications that can arise regardless of the type of SUI surgery employed, and other complications. The IFU is adequate. It indicates risks and avoidance of complications as well as details key procedural steps. The adverse reactions are the specific adverse events that could occur with the TVT, and the IFU tells physicians that pain can occur because pain is a symptom of the adverse events.

- The IFU for TVT appropriately indicates when it should be used as well as contraindications.

- In the IFU, Ethicon appropriately tells physicians how to tension the device and provides professional education on how to tension the TVT as well.

- Professional education supplements the IFU.

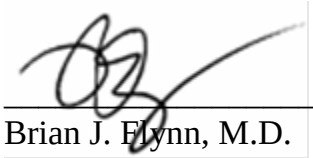
- Ethicon has a robust professional education program that addresses the procedure, clinical data, complication intervention and management. Ethicon had several phases of professional education for physicians. They may attend cadaver labs, preceptorship, proctorship, or several of these educational events. The professional education does not certify the competency of a physician.

- Professional education included discussion of complication management.

- The patient Brochure is not meant to supplant the informed consent process, but rather is a resource for additional information. It includes appropriate information on proper use, instructions, and adverse reactions.

- The patient brochure is a tool to facilitate a discussion with the patient and is not a substitute for the discussion between the patient and the physician. The 2009 patient brochure appropriately discusses the disease state, options, informs patients to consult with their physician, and identifies the necessary complications.

- Hospitals, professional organizations, and physicians are responsible for the credentialing of physicians.



Brian J. Flynn, M.D.

Dated: 5/31/2016